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California's Bioscience Industries: Overview and Policy Issues

By Daniel Pollak

Prepared at the Request of Assemblymember Howard Wayne Chair of the Assembly Select Committee on Biotechnology

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Executive Summary

The bioscience industries use cutting-edge knowledge and techniques from the life sciences to create commercial products and services. Many have predicted that these industries could radically transform virtually every aspect of our lives, from medicine to human reproduction, from industrial manufacturing to the food we eat.

The potential commercial applications are so extensive that state and local governments across the country are eagerly trying to cultivate the bioscience industries as engines of economic prosperity. At the same time, the advance of the biosciences causes concern, even fear, in some quarters, leading to controversies and calls for caution. The goal of this report is to provide an overview of California's bioscience industries, and to outline the actual and potential role of state policy with respect to these industries.

THE PROMISE OF THE BIOSCIENCE INDUSTRIES

The biosciences have delivered many important innovations, but these may be only a foreshadowing of things to come:

- *New kinds of medicine*. Genetic engineering has provided new ways to manufacture valuable medicines such as insulin and human antibodies. Hundreds of new biotechnology drugs are under development, targeted at a wide range of illnesses such as cancer, heart disease, and multiple sclerosis. Research into cloning and human stem cells could someday lead to advances in organ transplantation and the treatment of degenerative diseases such as Alzheimer's.
- *Medical devices*. Advances in materials science, engineering, computer science, and biology are coming together to bring us a host of sophisticated medical devices that are transforming the diagnosis and treatment of disease.
- *New kinds of food*. Genetically engineered varieties of corn, soy and cotton that resist pests or herbicides are already an important part of U.S. agriculture. These crops represent only a small fraction of the agricultural products that could be produced through biotechnology.
- *Industrial innovations*. Advances in biotechnology could transform industries such as chemical manufacturing and environmental cleanup.

PERILS OF THE BIOSCIENCE INDUSTRIES

If the bioscience industries arouse great hopes, they also arouse fears and controversy. These include concerns that genetically modified foods might be unsafe, and that genetically modified organisms could harm the environment. At the same time, a wide variety of critics worry that the biosciences could enable us to do things that are immoral, unethical, or could change our society in undesirable ways. For example, there are critics who worry about the ethics of using human embryos for research; or who question our growing ability to alter human biology (and perhaps human nature) through drugs and other medical innovations.

ECONOMICS AND GEOGRAPHIC DISTRIBUTION OF THE BIOSCIENCE INDUSTRIES

The bioscience industries are an important sector of the economies of the U.S. and California. However, the intense interest in them is due at least as much to their potential for growth as it is to their current stature.

California is the nation's leader in the biosciences, with more firms and employment in these industries than any other state. California is also the nation's leader in the private and academic research and development that drives these industries. In California, as elsewhere, the bioscience industries tend to form regional concentrations or "industry clusters." The San Francisco Bay Area and the San Diego region contain the largest concentrations in California. There are also large numbers of bioscience companies in other parts of California, such as the Los Angeles region, but they are more widely dispersed.

The advanced medical device field is the largest industry addressed in this report. However, pharmaceutical biotechnology has firmly established itself and is poised for rapid growth. The techniques of agricultural biotechnology are equally advanced and promise many new products, but that industry has been slower to grow, particularly in California. Among the chief obstacles faced by agricultural biotechnology are the controversies here and abroad over its alleged environmental and health risks, and resulting caution among food producers and marketers.

FUTURE PROSPECTS AND CHALLENGES TO GROWTH

There are a number of factors and challenges that bioscience companies typically confront. Such companies expend a great amount of capital on research and development. It takes a long time to develop new bioscience products and bring them to market, meaning that young companies often must operate for many years without revenues.

As a result, bioscience companies are heavily dependent on venture capital and other forms of investment to achieve commercial success. These financing sources often display a volatile "boom and bust" cycle, creating a climate of both opportunity and high risks.

There are strong reasons for optimism about the long-term growth of these industries. Particularly in its medical sectors, the bioscience industries are maturing rapidly with many promising new products in the development or regulatory pipelines. Basic scientific advances, such as the mapping of the human genome, have been arriving with startling rapidity.

PROBLEMS IN CALIFORNIA'S BUSINESS CLIMATE

Bioscience companies in California enjoy significant advantages that attract them to this state and keep them here. Chief among them are proximity to world-class universities and the critical mass of talent and support industries that characterize California's bioscience industry clusters. However, a number of issues are becoming a growing concern for their potential to inhibit future growth. These include deteriorating infrastructure, traffic, the cost of land and housing, costs imposed by regulation, and uncertainties about the cost and reliability of water and electricity.

In addition, California's educational system may be unable to meet the growing demand for a scientifically and technologically adept workforce. There are already indications that our K-12 system is not preparing enough students for scientific careers, a trend that is expected to deepen as the ethnic composition of the state changes and groups that have traditionally been under-represented in the sciences form a growing share of the population.

While California is likely to remain a leader in the biosciences for many years to come, the problems it faces could inhibit the growth of these industries in the state. For example, as biotechnology companies produce a growing array of pharmaceuticals, there is already a shortage of manufacturing capacity. Given the challenges of high land costs and other business climate issues, it is an open question whether the next generation of high-tech biopharmaceutical plants will be built in California or elsewhere.

THE ROLES OF GOVERNMENT

State and federal government influence the bioscience industries in many ways. The federal government provides billions of dollars for life science research and development (R&D) in the state, and California's government provides hundreds of millions of dollars for such R&D.

The state of California funds a variety of programs and policies that support the biosciences and other high-tech industries. Among these are economic development programs such as the state's six Regional Technology Alliances. The state and federal government provide a wide variety of tax incentives such as R&D tax credits that can be used by these industries.

By far the state government's most vital contribution to the bioscience industries is the support of the University of California system. University research is the wellspring of innovation that nourishes these industries. A great many California companies are commercializing inventions discovered by UC scientists. Furthermore, the entrepreneurs, managers and workers at these companies are very often UC graduates or current or former UC faculty.

The state of California has so far largely deferred to the federal government in regulating the biosciences with regard to the environmental and human health impacts of its

products. Such federal regulations can add significantly to the costs and time required to bring new products to market. While the federal regulatory process has been criticized for being slow and cumbersome to industry, some critics of biotechnology claim the system does not adequately protect human health and the environment. While the risks of biotechnology appear to be largely hypothetical at this point, many respected scientists have called for improvements in the federal regulatory system.

A MENU OF POLICY OPTIONS

If California's policy-makers decide to develop a strategy for dealing with the biosciences, they will be faced with a wide array of policy options. The range of options includes a number put forward to help the industries grow, such as:

- Creating or restructuring tax incentives to help the bioscience industries to grow;
- Addressing the infrastructure, land, and affordable housing issues that are hindering the bioscience industries in some regions;
- Providing grants, loans or other assistance to young companies to help them get through the lengthy and expensive product development process;
- Addressing problems in the process of licensing technologies from the UC system for commercial use ("technology transfer"); and
- Increasing support for basic K-12 science education; and increasing support for applied, vocational bioscience certificates and degree programs at the college and post-graduate level.

At the same time, some are less concerned with promoting these industries than in addressing perceived risks. For example, there are calls to require labeling of genetically modified foods, tighten regulation of the release of genetically modified organisms into the environment, or further restrict stem cell research and human cloning.

TOWARD A BIOSCIENCE STRATEGY

California's government is actively engaged with the biosciences on several fronts, but there are clearly many important unresolved issues. Policy-makers have the choice of maintaining the status quo, or of adopting some of the aforementioned policy options in an incremental fashion. A third alternative would be to follow several other states in developing a broad strategic plan for the biosciences. Any ambitious new plan for changing the state's role would require broad-based support. This would in turn likely require a systematic effort to assess the state's needs and goals, weighing the views of a variety of stakeholders in the process.

Introduction

Many have predicted that the bioscience industries could radically transform virtually every aspect of our lives, from medicine to human reproduction, from industrial manufacturing to the food we eat. The potential commercial applications are so extensive that state and local governments across the country are eagerly trying to cultivate the bioscience industries as engines of economic prosperity.

The predicted impact of the biosciences is often compared to that of computers in the 20th century. Yet in their capacity to provoke heated debate, the bioscience industries also sometimes draw comparisons to another technology that promised to transform the 20th century - nuclear energy. Opponents decry a variety of alleged dangers to human health or the environment, or raise concerns about manipulating nature in ways that are unethical or immoral. Defenders of the bioscience industries often accuse their opponents of fear-mongering and obstructing economic and technological progress.

Given the growing importance of these industries, the wide variety of challenges they face, and the competition from other parts of the country to attract these industries, it may be time for the state to develop a bioscience strategy. The goal of this report is to provide an overview of the information and issues that would likely be important if California is to develop such a strategy.

SCOPE OF THIS REPORT

This report focuses on the technologies that seem particularly relevant to policy-making because of their newness, their rapid evolution, and their potential for growing impacts in the coming years. The main topics will be medical and agricultural biotechnology, and the medical device industry. We will also touch upon industrial and environmental biotechnology, and recent developments in cloning and stem cell research.

This report will cover the following topics:

- What are the bioscience industries and technologies?
- The promise of the bioscience industries for technological innovation
- The perils that some see in the changes wrought by the bioscience industries
- The economic importance and geographic distribution of these industries
- Trends and challenges affecting their growth
- How government interacts with these industries
- Policy alternatives and options for the state

What are the Bioscience Industries?

This report is about industries that are sometimes collectively labeled "the biotechnology industry," a term that suggests a single kind of technology and a single industry. Instead we will use the term "bioscience industries." There are really a number of diverse (although related) technologies, used in a number of different (although related) industries. In this section we will briefly describe these technologies and how they are used. In the subsequent section, we will learn more about the innovations and benefits promised by these industries.

The bioscience industries use cutting-edge knowledge and techniques from the life sciences to create products or services. They include commercial applications of genetic engineering and other advances in biology in the fields of medicine, agriculture, and industry. In addition, we will consider the industry that uses advanced technology to create innovative medical devices.

We will reserve the term "biotechnology" to refer to applications of DNA science and technology. When the topic is broader (as when we are including medical devices) we will use the term "bioscience industries" or "biosciences."

BIOTECHNOLOGY

By the 1950s, scientists determined that biological inheritance was governed by the structure of deoxyribonucleic acid (DNA), long, threadlike molecules found in all living cells. By the 1960s, the structure of DNA was known, and scientists had unlocked the genetic code. The constituent molecules in the DNA strands form discrete, meaningful sequences known as genes. A gene is like a set of instructions for the molecular machinery of the living cell. The primary function of these instructions is to tell the cell how to assemble proteins from their building blocks, amino acids. The proteins then go to work as structural elements of cells and tissues, or as enzymes controlling further biochemical processes.

In the 1970s, scientists began learning how to cut and splice DNA, and introduce genes from one organism into another, even if the organisms belong to completely different species. Such alterations become part of the genetic code of the modified organism, and can be inherited when it reproduces. In this way, new organisms can be created with novel traits that could not be achieved through older techniques such as selective crossbreeding.

The term "recombinant DNA" is often used to describe the combination of genetic material from two different sources. This can happen naturally through sexual reproduction. In the biotechnology context, the term refers to combining genes from different sources through genetic engineering. Novel organisms produced in this way are sometimes called "transgenic" organisms or "genetically modified organisms" (GMOs).

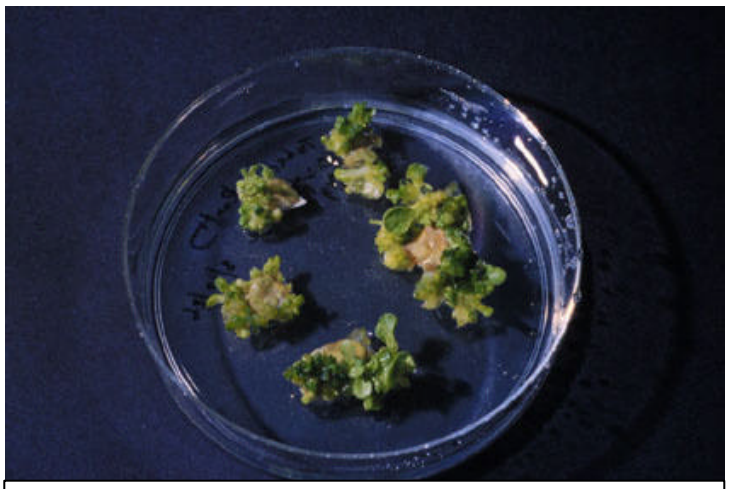
Medicines from Genetic Engineering

The most commercially important application of biotechnology so far is the use of genetic engineering to produce drugs and other medical treatments.

Biotechnologists take advantage of the fact that the cells of organisms are powerful biological factories capable of manufacturing a huge variety of complex proteins. Cells are able to manufacture substances that would be difficult to make in other ways, or difficult to make in sufficient quantities. After identifying a gene that produces a therapeutic protein, the gene is spliced into a cell line (cells from a plant, animal, or bacteria, grown in an artificial medium). The multiplying cells manufacture the needed substance, and the product is extracted. For example, the first biotech insulin was produced by inserting the human insulin gene into bacteria.

Transgenic Plants and Agricultural Biotechnology

Agricultural biotechnology is based on the use of genetically engineered plants and animals. Plants can be engineered to resist pests or disease, grow in adverse conditions, or produce crops with altered nutritional content.



Plant tissue culture grown for genetic engineering. (Fralin Biotechnology Center, Virginia Tech).

Similarly, animals can be genetically altered to grow faster, increase their yield, or produce novel products. Cloning, the creation of a genetically identical copy of an individual animal, may become an important component of animal biotechnology, allowing the creation of copies of individuals with valued traits.*

Human Cloning and Stem Cell Research

In the public debate over human cloning, "therapeutic" and "reproductive" cloning are often distinguished. "Reproductive cloning" would involve producing genetically identical copies of human beings. "Therapeutic cloning" is cloning human cells, especially stem cells, for scientific research purposes.

Few scientists advocate reproductive cloning, but many hope that stem cell research could eventually produce important medical breakthroughs in the treatment of disease, replacing damaged tissue and understanding human biology.

* It should be noted that in scientific parlance, "cloning" refers to more than just making genetic copies of animals. Cloning refers also to creating genetically identical molecules, cells, or plants. Molecular cloning is an essential foundation of all DNA technology.

Stem cells are early, undifferentiated cells from the cell masses that develop into embryos. Stem cells have the capacity to produce more of themselves, and can differentiate into a variety of cell types, such as blood, skin, heart or brain cells. Stem cells can be obtained through a variety of means, including aborted fetuses, embryos created *in vitro*, or through cloning of adult cells. However, the most promising, and the most controversial form of therapeutic cloning has been the cloning of human embryonic stem cells.

Industrial and Environmental Biotechnology

If plants and animals can be genetically altered to produce new foods or medicines, they can also be engineered to produce materials for industrial use, such as enzymes that could be used in chemical manufacturing processes. Genetically altered plants or microorganisms could be used to attack environmental contaminants.

INNOVATIVE MEDICAL DEVICES

The medical device industry encompasses a spectrum from high-tech to low-tech. At one end is the hospital supply field, which provides commodity-like products such as bandages or needles. At the other end are advanced medical firms.[1] Like biotechnology, the high-tech end of the medical device field is science-intensive, bringing together biology, physics, engineering, computer science, and new materials to treat or diagnose illness and injury. We will focus more on the faster-growing high-tech end of this industry.

Activity has accelerated with advances in new materials, information technology, and miniaturization. The science underlying new medical devices is highly interdisciplinary. Some of the basic research falls under the rubric "bioengineering," a field that applies physics, computing, engineering, and mathematics to understanding how physical structures in organisms work. For example, scientists are working on a computational model of the human heart, a project that could lead to advances in pacemakers and other therapies.[2]

The Promise of the Bioscience Industries

In describing the benefits that could be delivered by the biosciences, it is difficult to exaggerate the importance commonly attributed to them. For example, *Time* once called DNA technology "the most awesome and powerful skill acquired by man since the splitting of the atom."[3] The 21st Century has already been dubbed by some "The Bioscience Century."[4]

BIOPHARMACEUTICALS: THE LEADING SECTOR OF BIOTECHNOLOGY

Drugs produced through biotechnology are known as biopharmaceuticals. According to a recent report, as of 2000 there were 400 biopharmaceuticals in development, with 100 already on the market. So far, the top ten biopharmaceuticals account for nearly all the sales.[5] As the following table shows, biotechnology targets a great variety of diseases.

Table 1
Top 10 Biotechnology Drugs as of 2001
Ranked by Worldwide Sales

Product	Use	Developer
1. Procrit	Red blood cell enhancement for anemic patients	Amgen, Thousand Oaks, CA
2. Epogen	Red blood cell enhancement for anemic patients	Amgen, Thousand Oaks, CA
3. Neupogen	Restoration of white blood cells	Amgen, Thousand Oaks, CA
4. Intron A/ Rebetron	Hepatitis C, some cancers	Biogen, Cambridge, MAICN, Costa Mesa, CA
5. Humulin	Diabetes mellitus	Genentech, S. San Francisco, CA
6. Avonex	Multiple sclerosis	Biogen, Cambridge, MA
7. Enbrel	Rheumatoid arthritis	Immunex, Seattle, WA
8. Cerezyme	Enzyme replacement therapy for Gaucher Disease	Genzyme, Cambridge, MA
9. Rituxan	B-cell non-Hodgkin's lymphoma	IDEC, San Diego, CA
10. Synagis	Respiratory viral infections	MedImmune, Gaithersburg, MD

Source: Standard and Poor's 2001[6]

Increasingly, biotechnology is being used not just to manufacture known drugs, but to invent brand-new therapies. For example, the industry is beginning to see success with drugs called monoclonal antibodies, which are versions of natural human antibodies. Antibodies now in development target many conditions, including cancer, multiple

sclerosis, and organ transplant rejection. Without biotechnology, it would not be feasible to manufacture antibodies in commercial quantities.[7]

In addition to producing protein-based drugs, biotechnology has many other medical uses. Biotechnology can create new vaccines, perhaps one day even vaccines against cancer. DNA-based diagnostic tests can help to ascertain an individual's inherited disease risks.

(Photo courtesy of Fralin Biotechnology Center, Virginia Tech)

Advances in biotechnology and information technology are beginning to merge, a trend sometimes referred to by the name "bioinformatics." For example, scientists are using computers to analyze the vast number of ways that protein molecules can be folded into three-dimensional structures. Drugs targeted at folding abnormalities could help treat inherited diseases such as cystic fibrosis.[8]

Gene therapy is another important stream of biotechnology research. Gene therapy treats disease by administering synthetically manufactured genes, in order to supplement the action of the patient's genes or to block the function of harmful genes. Some gene therapy is targeted at inherited diseases or cancer. Other applications include an experimental gene therapy that could help a patient with blocked coronary arteries to grow new blood vessels.

Agricultural pharmaceuticals. Researchers hope that drugs that would be difficult to make in other ways could be harvested from genetically modified corn or the milk of transgenic dairy animals. Transgenic plants could also create novel drug delivery systems. For example, people in developing nations could someday receive vaccines by eating fruit or nuts grown with transgenic plants. Scientists are also trying to develop transgenic animals whose organs or tissues could be transplanted into humans without the risk of immune system rejection.

Forensic and anti-terrorism tools. DNA tests can be used to identify individuals for forensic and criminal investigations. Biotechnology is also being applied to new techniques for detecting, diagnosing, and neutralizing biological and chemical weapons.

AGRICULTURAL BIOTECHNOLOGY: A REVOLUTION IN THE MAKING?

The advent of agricultural biotechnology has been compared to the "Green Revolution" of the 20th Century, when mechanization, new hybrids, synthetic fertilizers, and other industrial techniques radically increased the world's ability to produce food. Biotechnology has been lauded as a comparable agricultural revolution.

Few products from agricultural biotechnology are being sold to consumers today. Yet those that have been commercialized are in wide use. The main transgenic crops are corn (26% of all corn grown in the U.S.), soy (68% of U.S. soy planted), and cotton (69%).[9] According to one estimate, more than 60% of all processed foods sold in the U.S. contain ingredients from transgenic soybeans, corn, or canola oil.[10] Much of our cheese today is produced with an enzyme, chymosin, that is manufactured using biotechnology.

Currently the most important transgenic crops are engineered for pest control purposes. These include crops that are herbicide tolerant, insect resistant, or resistant to pathogens (viruses, bacteria, and other plant diseases).

Another way to improve agricultural productivity is to create plants that can thrive in adverse climates or soil conditions – for example, biotechnologists are developing crops that could endure cold, frost, drought, or saline soils.[11]

While most genetically modified (GM) crops have been designed with the primary goal of increasing crop yield, the potential applications go beyond productivity – agricultural biotechnologists hope to reduce agriculture's impact on the environment and create new foods with improved taste, quality and nutritional value.

A field of herbicide-tolerant soybeans. (Photo from University of Maine Cooperative Extension).

For example, researchers have developed "golden rice," a strain of rice that synthesizes beta-carotene.* The developers believe such rice could remedy the vitamin A deficiencies and resulting blindness that affect hundreds of thousands of children in Southeast Asia.[12] Genetically modified oil seeds could be used to promote health and prevent disease – for example, natural margarines could be made without unhealthy trans-fatty acids.[13]

* The "golden" color is due to the accumulation of this beta carotene.

Table 2
Transgenic Crops Approved for Commercial Use (as of June 2002)

Crop	Altered Traits
Corn (15 varieties)	Herbicide Tolerance (9 varieties) Insect Tolerance (9 varieties) Male Sterility (3 varieties)*
Potato (5 varieties)	Insect Resistance (5 varieties) Viral Resistance (3 varieties)
Flax (1 variety)	Herbicide Tolerance
Rice (1 variety)	Herbicide Tolerance
Rapeseed (canola) (4 varieties)	Herbicide Tolerance (3 varieties) Altered pollen (1 variety)* Altered Oil Composition** (1 variety)
Chicory (1 variety)	Male sterility
Soybean (5 varieties)	Herbicide Tolerant (4 varieties) Altered Oil Composition*** (1 variety)
Tomato (10 varieties)	Delayed ripening
Beet (2 varieties)	Herbicide Tolerance
Papaya (1 variety)	Viral Resistance
Squash (2 varieties)	Viral Resistance
Cotton (5 varieties)	Insect Resistance (2 varieties) Herbicide Tolerance (4 varieties)

Source: Information Systems for Biotechnology[14]

NOTES:

**Plants with sterile male flowers cannot self-pollinate, a useful trait for some crop breeding techniques
**The altered canola oil has a higher laurate content, a fatty acid used in making soap and detergent
***High oleic oil, useful for industrial applications

DNA Sequencing to Enhance Plant Breeding

Wild relatives of commercial crops often have desirable traits such as disease resistance or improved fruit quality. Genomic sequencing can identify the genes behind such traits, or identify markers associated with them. Using these markers, cross-breeding the trait into the commercial strain can be accomplished with much improved speed and precision. And unlike genetically engineered crops, the new variety need not undergo the federal regulatory process for transgenic plants.[15]

Possible Uses for Transgenic Animals

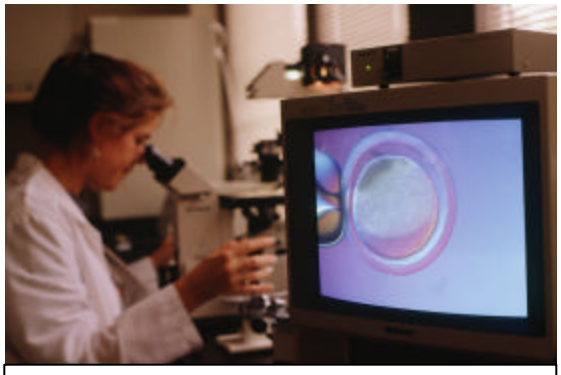
Creating a new kind of animal is more difficult than creating a genetically altered bacterium or plant. Nevertheless, biotechnologists are working on new lines of animals, such as faster-growing pigs, sheep that grow more wool, or cows that produce milk that ripens into cheese faster.[16]

As noted earlier, genetically altered animals provide pharmaceuticals or tissues for medical purposes. There are also industrial applications – for example, using the milk from transgenic goats to produce spider silk (a potentially valuable industrial material for products like bulletproof vests or surgical sutures).[17]

THE PROMISE OF STEM CELL RESEARCH

The National Institutes of Health has identified three promising avenues of stem cell research:[18]

Generate cells and tissue for transplantation. Stem cells have the potential to develop into specialized cells that could be used as replacement cells and tissues to treat diseases and conditions, including Parkinson's disease, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.



Genetic manipulation of an animal cell. (Fralin Biotechnology Center, Virginia Tech).

Advances in developmental biology. Studying stem cells could improve our understanding of the complex process of human development and help uncover the causes birth defects and cancer.

Improve drug testing. Rather than evaluating the safety of candidate drugs in an animal model, drugs might be initially tested on cells developed from stem cells, allowing us to test only the safest candidate drugs on animals or humans.

FUTURE BENEFITS OF INDUSTRIAL, ENVIRONMENTAL, AND OTHER BIOTECHNOLOGIES

Although the high-profile applications of biotechnology are currently in food and medicine, some observers think that the industrial applications could eventually have an equally profound impact. According to one industry analyst, "Biotechnology … is not going to be about food, it's going to be about using renewable, nonpolluting resources to produce innovative products that will be as much a part of our lives as plastics and computers are now."[19] Some examples of industrial and environmental biotechnology:

New materials. Biotechnology could help produce materials from plants that would serve as renewable, environmentally friendly alternatives to petroleum-based plastics.[20]

Production of chemicals. Genetically altered organisms can produce useful enzymes and catalysts for uses ranging from the manufacturing of detergents to the production of biomass energy.[21]

Improved manufacturing. Enzymes produced through genetic engineering could reduce the environmental impact of manufacturing paper and textiles.[22] Seed oils from agricultural crops such as canola could be modified for a variety of industrial purposes such as the making of biodegradable soaps or lubricants.[23]

Environmental cleanup. Genetically modified organisms could be employed to treat wastes or contamination.

THE PROLIFERATION OF INNOVATIVE MEDICAL DEVICES

The high-tech end of the medical device field includes diagnostic devices such as echocardiography, positron emission tomography scanning, three-dimensional echo techniques and magnetic resonance imaging.[24] It includes new therapies such as using lasers or other devices to perform minimally invasive surgery.[25] It also includes a wide variety of implants, such as devices that deliver medications or assist the heart in pumping blood, [26] or synthetic skin substitutes for burn victims.[27]

Medical informatics is a related field that uses information technology to process medical data for diagnosis and problem-solving, from the level of cells and genes up through patients and populations. For example, doctors are experimenting with using computer assistance to detect abnormalities on mammograms. Another aspect of medical informatics is the use of digital imaging and the Internet to transmit data such as brain scans. This can speed diagnosis and allows doctors to collaborate over long distances.[28]

Another growing area for medical devices is in "home-care systems." These systems allow patients to monitor themselves with devices that warn of problems or monitor the status and treatment of chronic conditions. A related development is "telemedicine," in which images and sound carried by telephone lines displayed on computer or TV monitors allow patients to be examined remotely by nurses or physicians who are many miles away.[29]

Nanotechnology

One trend in medical technology is the creation of smaller and smaller devices. For example, one company has produced a capsule, the size of a pill, containing a tiny camera that a patient swallows. The camera transmits video signals so that physicians can diagnose problems in the gastrointestinal tract.[30]

This trend toward miniaturization could eventually come to full fruition with medical nanotechnology, the construction of medical devices at the molecular scale.* Nanotechnology is an emerging field of research that could some day revolutionize all forms of technology, not the least, medical technology. However, these revolutionary applications are still mostly speculative and probably many years away from realization.

Nanotechnology experts believe the technology could someday produce computers the size of a grain of dust or robots that travel in the human bloodstream to repair damaged tissue or attack tumors.[31] Nano-scaled drug delivery devices and sensors could someday treat or diagnose disease inside the body.

* The name derives from the "nanometer," a unit of measure equal to one billionth of a meter (a human hair is tens of thousands of nanometers in width).

The Perils of Biotechnology and the Biosciences

The biosciences hold great promise, but have also provoked some fears and concerns, most notably:

- Are genetically modified foods safe and healthy?
- Could the products of the biosciences harm the environment?
- Will the biosciences allow us to do things that are immoral, unethical, or change our society in undesirable ways?

HEALTH AND SAFETY OF GENETICALLY MODIFIED FOOD

In the earliest days of genetic engineering (the late 1970s), some scientists worried that tampering with the genes of bacteria and viruses in the laboratory could inadvertently unleash new pathogens (infectious diseases) on humanity. Such fears about the safety of laboratory work with DNA have largely abated, and it is widely accepted that under current standards the manipulation of DNA in the laboratory is not particularly dangerous.[32]

Nowadays the main health and safety debate concerns genetically modified foods (sometimes called "GM foods"). A number of consumer and environmental groups have argued that such foods may be unsafe and have not been sufficiently tested.[33] They warn that altering the genetic makeup of crops could inadvertently introduce allergens, toxins or carcinogens into our food. Another worry is that bioactive molecules produced by GM crops or livestock, such as chemicals affecting growth or metabolism, could retain their bioactivity in humans after being consumed.

The debates about the safety of GM food revolve around not only facts but also regulatory philosophies. In particular, there are two core issues: the *precautionary principle* and the question of *product versus process.*

The Precautionary Principle

The precautionary principle, a maxim of the environmental movement, holds that caution should rule in the face of scientific uncertainty about the effects of a new technology.[34] Accordingly, say many environmentalists, the burden of proof should be on proponents of biotechnology to demonstrate its safety before exposing large numbers of people and the ecosystem to its potential risks.

Supporters of biotechnology tend to argue that the precautionary principle is being misused to stigmatize GM foods and stifle innovation when there is no scientific basis for doing so. They note GM foods have been consumed safely for several years, and that such foods are already regulated by the federal government more rigorously than other new food crops produced by conventional breeding.[35]

Process Versus Product

A related core issue of the controversy is the question of *process versus product*. Critics of biotechnology often argue that there are inherent risks in the *process* of applying genetic engineering to foods. They point to the ability to combine genes from radically different species, introducing traits that couldn't possibly be achieved through normal breeding and that have not been present in the food supply before. They further argue that the results of genetic engineering are sometimes unpredictable.

Supporters of GM foods retort that we should be concerned with the *product,* not the process. We might call this the "a potato is a potato" argument. In the absence of specific concerns about the safety of GM food, the mere fact that it was genetically engineered should not raise any particular concern. They point out through centuries of cross-breeding and hybridization, all our food crops have been altered genetically. Plant breeders even introduce new genes through mutations induced by chemicals or radiation, without causing great controversy (and with less regulatory oversight than is required for genetically engineered crops). Supporters argue that the process of genetic engineering introduces fewer new genes, and in a more controlled manner than these other methods.

Is the Food Safe?

While some opponents have labeled foods derived from engineered crops as "Frankenfoods," the dangers of GM foods to human health seem to be primarily hypothetical at this point. For example, there do not appear to be any documented cases so far of a person dying or becoming seriously ill from an allergic reaction caused by the genetic alteration of a food crop.[36]

Scientists debate how to evaluate the possible risks of GM foods (a topic we will return to later). At the same time, however, there is a broad consensus among scientists that it is not dangerous to consume the GM products currently on the market, especially when compared to more clearly documented contamination risks such as from bacteria or other pathogens.

For example, the U.S. General Accounting Office conducted a study that reviewed the literature and consulted experts in government, academia, consumer groups, and the private sector. The study concluded that the current system of federal tests for food safety was adequate for biotechnology crops, and that the foods produced in this manner presented similar risks to conventional crops.[37] The American College of Nutrition recently reached similar conclusions.[38]

There are dissenters from this viewpoint. For example, the environmental organization Greenpeace has stated, "We know that allergies can transfer unexpectedly from genetic engineering. We know that levels of toxins in food can also increase…We are currently in a situation in which biotechnology industries are trying to turn the burden of proof on its head, in which their risky technologies are deemed innocent until proven dangerous."[39]

While there is not widespread alarm among scientists, many of them believe these issues deserve further consideration and study. Few dispute that it is at least possible for genetic modification to inadvertently introduce allergenic or biologically active new substances into food. And some prominent scientists have noted that as the number, variety, and complexity of modified traits increases, it will become increasingly difficult to predict what effects the changes might have. It is likely we will increasingly see the introduction of substances into food about which we have little data or experience regarding human allergens or other biological effects.[40]

COULD THE NEW TECHNOLOGIES HARM THE ENVIRONMENT?

The biosciences are, generally speaking, fairly clean industries. Like other industries, they may produce waste products in the form of toxic wastes, air emissions or wastewater. Some biomedical research produces low-level radioactive wastes, the disposal of which has been a thorny issue for some time.[41]

However, by far the most debate has to do with whether transgenic organisms threaten the environment. As with food safety, the opposing arguments often revolve around the application of the precautionary principle and the process versus product question. In short, the environmental risks of transgenic organisms are to a large degree hypothetical, leading to questions such as, *Is there anything inherently risky about an organism produced through genetic engineering, in comparison to other types of organisms?* And, *Would stronger regulation be a rational response to uncertainty, or a needless chilling of a promising new technology?*

There are a number of distinct environmental issues, including:

- Transfer of genes to wild populations, and escaped transgenic organisms
- Unintended effects of the transgenic organism on other organisms
- Impacts on the world's agricultural systems
- Misuse of nanotechnology

Transfer of Genes to Wild Populations

Critics of biotechnology worry about gene flow, the transferring of genes through interbreeding between cultivated transgenic organisms and their wild relatives. For example, one scenario is that pollen from herbicide-tolerant crop plants might fertilize related species of wild weeds, creating herbicide-tolerant "superweeds."

Supporters of biotechnology tend to argue that these risks are very small or virtually nonexistent, and are adequately addressed by current federal regulations. They point out that in the United States, many of the transgenic crops are not cultivated in proximity to wild plants with which they could interbreed. They argue that domestic plants and animals are generally not well-adapted for life in the wild, so it is unlikely that hybrids of transgenic domestic organisms with wild organisms would result in hardy offspring.

A similar concern is that the transgenic organisms such as fish, insects, or microorganisms could escape and spread into the environment with harmful effects. A recent report from a panel of the National Academy of Sciences called for more attention to this danger. The panel expressed particular concern about aquatic organisms and insects "because their mobility poses serious containment problems and because, unlike domestic farm birds and mammals, they can easily become feral and compete with indigenous populations."[42]

This debate has recently focused on transgenic fish such as salmon, which may soon be commercially grown in aquaculture. According to some scientists, wild species of fish could be wiped out if they interbred with the transgenic fish.[43]

Unintended Effects on Other Organisms

In addition to the concerns about gene flow, some critics of biotechnology worry that the modified organisms will have adverse impacts on other organisms. The monarch butterfly has become emblematic of this debate. In 1999, scientists at Cornell University and at Iowa State University announced experimental results suggesting pollen drifting from a field of corn engineered to produce an insecticide called Bacillus thuringiensis (Bt) might poison monarch butterfly larvae living nearby.*

These studies generated considerable controversy. More recent research indicate little risk to the butterflies under natural conditions. One variety of Bt corn did produce potentially toxic concentrations in its pollen, but that variety had never been used widely and was soon phased out.[44]

Another question about Bt crops is the risk of creating Bt-resistant pests. It is possible that the use of Bt crops could cause the targeted pests to develop resistance to the pesticide over time through natural selection. Federal regulators have tried to develop rules governing how such crops are planted to control this potential problem.[45] This issue is of particular concern to organic farmers, who rely heavily on Bt pesticides.

Impacts on the World's Agricultural Systems

Some of the opposition to biotechnology arises from fears about how the new technology will impact agricultural practices. Often opponents claim that GM crops consolidate control of seed lines in the hands of a few large corporations. Some claim that this could erode agricultural biodiversity or undermine small farmers. Some opponents are opposed to industrial agriculture, with its dependence on synthetic fertilizers, pesticides, and petrochemicals, and associate biotechnology with that system.

Critics also raise concerns about whether agricultural biotechnology can comfortably co-exist with other agricultural practices. Organic farmers worry that GM crops will cross-fertilize with non-GM crops. The demand in some domestic and export markets for GM-

* Bt is a natural insecticide produced by plants altered with a gene from a bacterium known as Bacillus thuringiensis. It is the most common form of genetically engineered insect-resistance.

free products could require keeping transgenic and non-transgenic food products separate throughout the entire food production chain.[46]

The possibility of cross-pollination of non-GM crops with GM strains also raises fears about the protection of agricultural biodiversity. For example, there is currently an acrimonious debate among scientists about whether genetically engineered corn has interbred with indigenous Mexican corn. Such indigenous varieties are considered vital reservoirs of the agricultural gene pool because they provide plant breeders with useful traits such as disease resistance. Some of the original claims about the Mexican corn contamination have been thrown into doubt by other scientists, but the debate continues.[47]

Should We Be Worried About GMOs in the Environment?

A panel from the National Academy of Sciences studied many of these issues in the 1980s, and their conclusions still reflect the thinking of much of the scientific and regulatory community in the United States. They found that "there is no evidence that unique hazards exist either in the use of [recombinant DNA] techniques or in the transfer of genes between unrelated organisms." The NAS study did not conclude that there were no risks, but rather that these risks were "the same in kind as those associated with the introduction into the environment of unmodified organisms and organisms modified by other genetic techniques."[48] In other words, we should be cautious about introducing such organisms into the environment, just as we should be cautious about things such as releasing exotic or potentially invasive species into the environment.

Critics of biotechnology argue that transgenic organisms are different, because of the ability to combine genes from widely disparate species and the power to add traits to species that could not be introduced by other breeding techniques.

Environmental Benefits of Agricultural Biotechnology

Supporters of biotechnology are quick to argue that while many of the environmental dangers of biotechnology are still hypothetical, engineered crops may have some real and immediate environmental benefits.

Proponents of biotechnology claim that transgenic crops reduce the use of harmful pesticides and herbicides. The Bt pesticide in pest-resistant crops is one of the most environmentally benign pesticides, was already widely used, and is nontoxic to humans. The glyphosate herbicide used with herbicide-tolerant crops is also considered one of the most environmentally benign herbicides.

Biotechnology supporters also point out that a growing world population will need ever more food, and that increased crop productivity through biotechnology could reduce the need to convert natural habitat into agricultural land in parts of the world where arable land is in short supply.

Perhaps the most ambitious effort so far to quantify environmental benefits is a recent study by the National Center for Food and Agricultural Policy (NCFAP). The study

estimated that the use of eight GM crops in the U.S. (varieties of papaya, squash, canola, soybean, corn, and cotton) resulted in the use of 45.7 million fewer pounds of pesticide in one year (2001).[49] (According to U.S. EPA, U.S. agriculture uses about 722 million pounds of pesticides annually).[50] Similar reductions of tens of millions of pounds of pesticide use could occur in California, according to the NCFAP study, with the adoption of other GM crops that have already been developed.[51]

Critics of biotechnology tend to dispute such estimates. The environmental effects of farming with transgenic versus non-transgenic crops is a contentious and complex subject. The comparison depends on numerous variables relating not only to the crop but also the region and variations in farming practices.[52]

Perils of Nanotechnology

Nanotechnology is such a new field that debates about its safety are highly speculative. Some environmentalists have begun to raise questions about the potential impacts of releasing toxic "nanoparticles" into the environment, although other scientists say the problem would not be fundamentally different from managing other kinds of industrial chemicals.[53]

However, some prominent futurists are worried that when nanotechnology matures it could be a dangerous tool in the wrong hands. Nanotechnologists envision the ability to someday create microscopic, self-replicating machines that could multiply with the rapidity of microbes. Sun Microsystem's chief scientist, Bill Joy, recently announced that he would not work on nanotechnology. He suggested scenarios under which self-replicating nanomachines, perhaps designed as weapons, could someday wipe out human life, or perhaps all life on earth.[54]

ETHICS, MORALITY, AND SOCIAL IMPLICATIONS OF THE BIOSCIENCES

The biosciences pose numerous ethical and moral questions. These include:

- Altering human biology and human nature
- Manipulating the natural world
- New social and economic inequities
- Privacy and control of genetic information

Altering Human Biology and Human Nature

Biotechnology promises to help individuals to escape normal constraints of human biology. Cloning, genetic engineering, and the extension of the human lifespan bring difficult moral questions into the policy arena.

Human Cloning and Stem Cell Research

There is a wide scientific consensus that reproductive cloning at present would be an unethical experimentation on human subjects. To begin with, many clones have suffered

fatal complications such as premature aging, immune system failures, and sudden unexplained deaths.

Even if scientific advances make human cloning safe, there are a variety of ethical concerns. Cloning humans has been called a debasement of the sanctity of human life. According to one line of thinking, cloning would violate the dignity and rights of the resulting child who would be deprived of genetic individuality. At least one widely-read pundit recently warned we were not far from the day that scientists might try to create a weird hybrid of apes and humans.[55]

What of non-reproductive, "therapeutic" cloning of human embryonic cells or tissue for research? There is the 'slippery slope' argument – that therapeutic cloning would ultimately lead to other forms of cloning. President Bush stated that allowing therapeutic cloning "would be taking a significant step toward a society in which human beings are grown for spare body parts, and children are engineered to custom specifications; and that's not acceptable."[56]

A further ethical argument against therapeutic cloning, is the claim that the embryos created, and destroyed, are entitled to some or all of the protections normally afforded to human life. As President Bush stated, "Research cloning would contradict the most fundamental principle of medical ethics, that no human life should be exploited or extinguished for the benefit of another."[57]

Cloning has given rise to an unusually broad opposition coalition. Liberal environmental, health, and bioethics advocates often find themselves on the same side of the issue as religious conservatives and anti-abortion activists.

Human therapeutic cloning has broad support in the scientific community. Among the general public, however, there is considerable opposition, especially when embryos are involved. According to a Gallup poll, 61% of Americans opposed the use of cloned human embryos for medical research, while 51% favored "cloning of human cells from adults" for use in research.[58]

Alteration of 'Human Nature'

Other applications of biotechnology raise fears that biotechnology is going to allow us to engineer fundamental changes in human nature. While in general these capabilities do not yet exist, they are plausible extrapolations of current trends.

Advances in neuropharmacology and genomics* could enable us to create designer drugs tailored to alter an individual's mental states. Human life as we know it would be greatly

* "Genome" is the collective term for all the genetic material found in the chromosomes of a given organism. Genomics sequences the DNA in the genome, identifies genes, and seeks insights into the role genes play in the growth, structure and functioning of living organisms. The most highly visible fruit of genomics has been the sequencing of the entire human genome (the "Human Genome Project"), an endeavor that will help scientists investigate the genetic basis of human biology and disease.

altered if unwanted emotional states and personality traits could be medicated away. In one hypothetical future, "Stolid people can become vivacious; introspective ones extroverted; you can adopt one personality on Wednesday and another for the weekend."[59]

The biosciences also promise to greatly extend the human lifespan, by curing diseases, manufacturing transplants of organs or tissue, and unlocking the mechanisms of cellular aging. Those who could afford to prolong their lives indefinitely might "just refuse to get out of the way, not just of their children, but their grandchildren and great grandchildren."[60]

Biotechnology seems to offer the potential to genetically alter our offspring, or at least screen embryos for desired traits. There is something repugnant to many in the idea of trying to use scientific methods to control the genetic makeup of human babies. To some, it raises the specter of discredited racist philosophies and eugenics, the idea of improving the human race through the control of reproduction. It strikes some as an arrogant appropriation of a power that should be left to God or nature.

Many would agree that such fundamental changes should not be embraced without some caution. As suggested by the title of a recent book, *Our Posthuman Future*,[61] we are faced with the potential to change human nature itself.

Manipulation of Nature

The ability to manipulate and redesign organisms at the genetic level raises profound questions about the relationship between human beings and nature, and whether we are changing it in undesirable ways.

Many of these ideas have been articulated by Jeremy Rifkin, an author/activist who often points out that our technological prowess is increasingly turning life itself into an object to be manipulated or commodified.

> The new genetic science raises more troubling issues than any other technology revolution in history. In reprogramming the genetic codes of life, do we risk a fatal interruption of millions of years of evolutionary development? Might not the artificial creation of life spell the end of the natural world? … How will the patenting of life affect our deepest convictions about the sacred nature and intrinsic value of life? What is the emotional and intellectual impact of growing up in a world where all of life is treated as "invention" and "commercial property?[62]

New Social and Economic Inequities

Some worry that the biosciences will reorder society in harmful ways, exacerbating existing inequities or creating new ones. Supposing we develop the ability to create designer babies, extend the human life span, cure diseases, slow the aging process, and so

forth. Who will be able to afford these things, and what will be the impact if they are reserved for only the affluent?

Another major strand of debate concerns who controls the direction and ownership of new bioscience technologies. As already noted, some critics of agricultural biotechnology view it as a force for consolidation of control of agriculture by large corporations, and as a threat to alternative farming practices such as small family farms, indigenous agriculture, or organic agriculture. Furthermore, they point out that while biotech companies can gain proprietary rights and profits by making minor variations in crops such as corn, no system exists to compensate farming communities around the world for the creation of the original crop varieties that form the basis for these products.[63]

Related ethical concerns also arise with regard to the patenting of useful genetic sequences. Some argue that genes, particularly human ones, should not be patentable at all, either out of respect for human rights or a belief that such natural phenomena should remain a public good.

Privacy and Genetic Information

The ability to test for genetic defects has raised questions about privacy and the ability of government, employers or insurers to access and use personal genetic information. Common uses include neonatal testing for susceptibility to genetic diseases, and pre-natal amniocentesis to detect Down's Syndrome. In some cases, the test indicates that the person will develop a disorder, in others merely that he or she is a genetic carrier for the trait who could develop it or pass it to offspring.

Privacy, consumer, and patients' advocates are concerned that individuals retain confidentiality and control over disclosure of genetic information, which would be of interest to many parties, such as employers and insurers.

Economic Importance of the Bioscience Industries

BELIEVE THE HYPE?

The bioscience industries are an important sector of the economy. Many believe that the biosciences will provide the next great knowledge-based industries, analogous to the role of information technology in the economy of the late 20th century.

Medical biotechnology in particular grabs more headlines than might be expected based on its current size. But the interest in the bioscience industries is due not to mere size but to their potential for growth and the growing impact of their products. In the recent past, the bioscience industries have grown and matured substantially. In the near-term, many new products are well along in the development pipeline. The aging of the U.S. population promises a growing healthcare market. In the longer term, these industries seem to promise boundless possibilities for technological innovation.

The bioscience industries attract a great deal of attention not only from the investment community, but from state and local governments as well. Many states and regions are attracted by the promise of a clean industry that promises continual innovation, wealth generation, tax revenues, well-paying jobs, and a variety of support industry spin-offs.

As a result, many states across the country are vying to attract and strengthen their bioscience industries. At least forty-one states have launched initiatives to support and grow the biotechnology industry.[64] Many of them are investing substantial resources in tax incentives and other incentives in the hopes of creating something like California's Silicon Valley. In a separate survey of 77 local and 36 state economic development agencies, 83 percent listed biotechnology as one of their top two targets for industrial development.[65]

HOW LARGE ARE THE BIOSCIENCE INDUSTRIES AND WHERE ARE THEY LOCATED?

By most measures, California is the leading state in the country for the bioscience industries.[*] To give a sense of how bioscience industries are distributed around the country, the following tables show the top ten states in three areas: medical biotechnology, the medical device industry, and agricultural biotechnology.

[*] Good statistics about the bioscience industries can be hard to come by. Because of their newness, some of its sectors, particularly in biotechnology, are not well-reflected in the system of industrial classification used by the U.S. census and other government agencies. As a result, much of the available data comes from private sources, and different sources use different definitions and methods. We will in each case identify where the data came from and the definition of biotechnology that it is based upon.

Table 3
Medical Biotechnology Firms: The Top 10 States by Number of Firms *

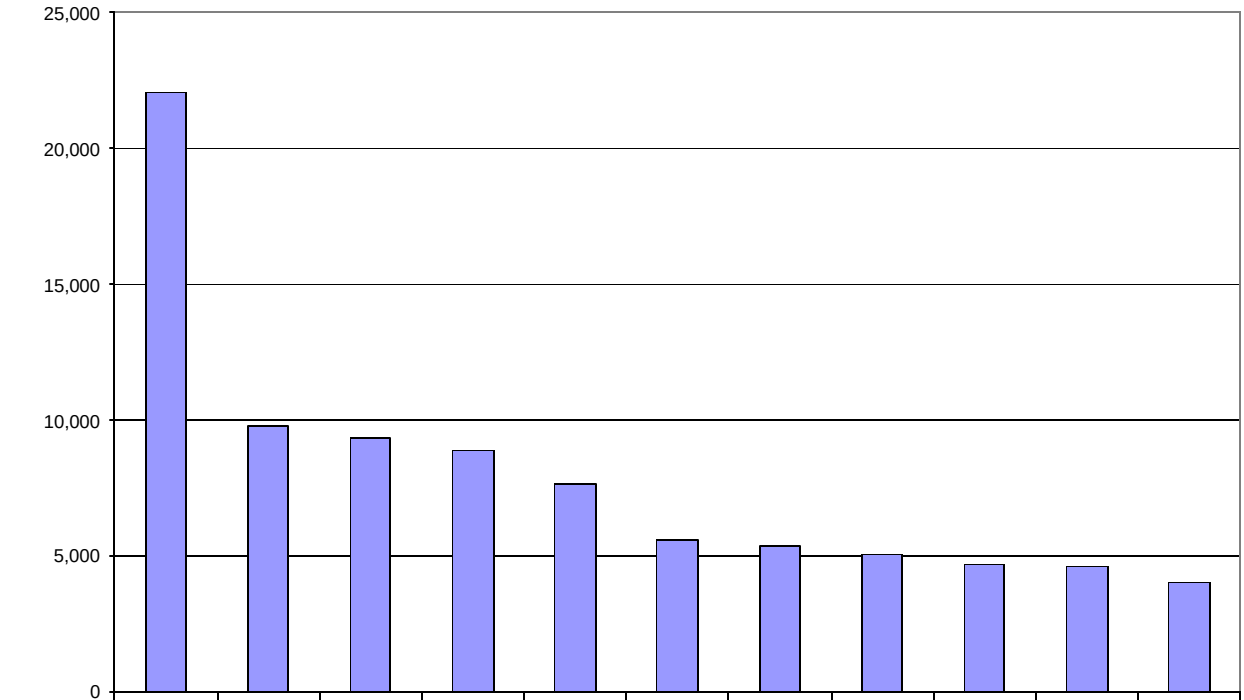
Rank	State	Number of Companies
1	California	410
2	Massachusetts	210
3	Maryland	95
4	North Carolina	87
5	Pennsylvania	71
6	New Jersey	69
7	New York	68
8	Washington	41
9	Georgia	37
10	Texas	36

Source: Ernst & Young 2002[66]

As for medical devices, comparative data on the number of such firms in different states is not readily available. However, an indication of how different states stack up in this industry can be gleaned from employment data gathered by the U.S. Census.

* These data, compiled by Ernst & Young, tally companies involved in drug development and manufacture, diagnostics, and related services and research such as genomics and proteinomics. They do not include agricultural, industrial and environmental biotechnology or the medical devices field. They also do not include pharmaceutical companies that do in-house biotechnology research, unless it is via a separately traded subsidiary.

Figure 1
Medical Device Industry: The Top States by Employment*



	California	Minnesota	Mass.	Florida	New York	Wisconsin	Illinois	Utah	Colorado	Washington	Penn.
Employees	22,050	9,813	9,367	8,862	7,644	5,585	5,371	5,031	4,671	4,605	4,012

Source: U.S. Census 2000 County Business Patterns

In some important respects, California is *not* the leader in agricultural biotechnology. For one thing, most of the intellectual property rights for the dominant biotechnology crops now in use are controlled by several large agribusiness corporations that are based outside of California, such as Monsanto and Novartis.[67]

Furthermore, of the 22 states growing transgenic crops, California grows the least amount. The only transgenic crops widely grown in California are cotton and corn. In 2001, 36% of the upland cotton grown in California was genetically modified for pest resistance or herbicide tolerance (about 233,000 acres).[68] That same year, about 13% of the corn grown in California was engineered for herbicide tolerance (about 30,000

* This table presents data for the following NAICS industry classifications: 339112 (Surgical and Medical Instrument Manufacturing), 339113 (Surgical Appliance and Supplies Manufacturing), 334510 (Electromedical and Electrotherapeutic Apparatus Manufacturing), 339114 (Dental Equipment and Supplies Manufacturing), 334517 (Irradiation Apparatus Manufacturing), 339115 (Ophthalmic Goods Manufacturing). For some states, a range (high and low estimate) was averaged to provide a single point estimate.

acres).[69] The leading state for production of transgenic crops was Iowa, which planted over 13 million acres of transgenic corn and soy in 2001.[70]

California does, however, lead the nation in the number of companies developing agricultural biotechnology. According to data compiled by a U.C. Berkeley scholar, as of 1999, there were 228 agricultural biotech companies in the United States.[71] The top 10 states, in terms of number of companies in that list, are shown below in Table 3.

Table 4
Agricultural Biotechnology Firms: The Top 10 States as of 1999*

Rank	State	Number of Companies
1	California	44
2	Wisconsin	15
3	North Carolina	12
4	Illinois	11
5	New Jersey	10
5	New York	10
6	Iowa	9
6	Michigan	9
6	Minnesota	9

Source: Gregory Graff, U.C. Berkeley

Revenues and Employment

The bioscience industries provide a significant source of revenues and well-paid employment for California. These industries will become more important as they continue to grow.

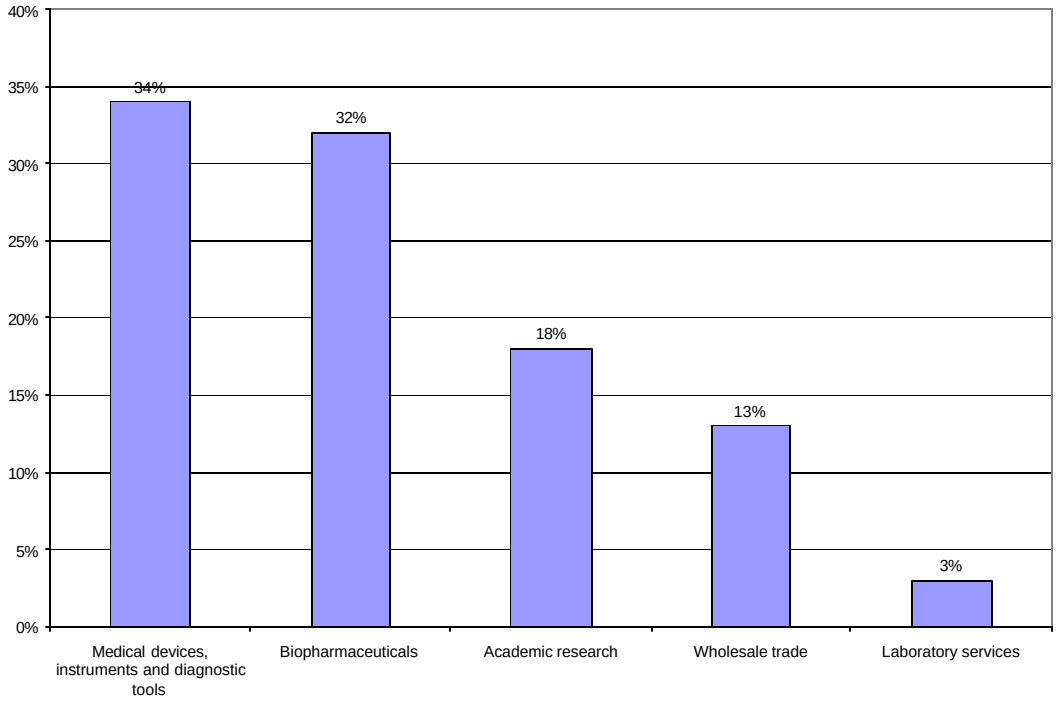
Employment

The largest categories of employer in California's biomedical industries are medical devices and biopharmaceuticals (pharmaceuticals derived from living organisms or their components).

* The author of this data is a graduate student in U.C. Berkeley's Department of Agricultural and Resource Economics.

According the California Healthcare Institute (CHI), a healthcare technology industry organization, 225,000 Californians worked in the biomedical industry, earning $13 billion in wages and salaries, in 2000.[72*]

Figure 2
Breakdown of Employment in California Biomedical Industries



Source: California Healthcare Institute 2002[73]

The jobs provided by the bioscience industries have broader ripple effects in the economy. According to Ernst & Young, medical biotechnology directly employed 150,800 employees nationwide in 1999. Using economic input-output models, Ernst & Young estimated indirect and induced impacts accounted for an additional 287,000 jobs.[74†]

* CHI defines biomedicine broadly, including both companies that manufacture and wholesale medical products and services. Products and services covered include pharmaceuticals, DNA technology companies, medical devices, makers of medical laboratory and analytical equipment, and medical research facilities.

† Indirect impacts are the result of purchases made by the industry from other industries, such as computer and equipment manufacturers and contract research organizations. Induced impact is the impact created by the purchases of workers and owners in the biotech and supporting industries.

Bioscience jobs tend to be well-paid. For example, an industry organization estimates that the median wage of life science jobs in San Diego region is $65,000.[75] The average wage for a job in California in 2000 was $40,367.[76]

Revenues

The medical device industry is probably the largest revenue-earner of the bioscience industries. It represents a worldwide market of about $170-175 billion, according to Standard & Poor's. Standard & Poor's estimates that in 2005 the medical device industry will have sales of $35 billion in the United States.[77]

In California, biomedical companies had $7.8 billion in revenue in 2000, according to the California Healthcare Institute.[78] Nationwide, biotechnology (which is a subset of biomedicine) produced $25 billion in revenues in 2000, according to one estimate.[79]

California's Bioscience "Clusters"

The bioscience industries tend to grow into regional concentrations that are often termed "industry clusters." An industry cluster includes companies of a particular industry, together with the supporting network of related service and supply industries, research institutions and infrastructure. This phenomenon is not unique to the biosciences. The congregation of information technology companies in the Silicon Valley provides one of the best known examples.

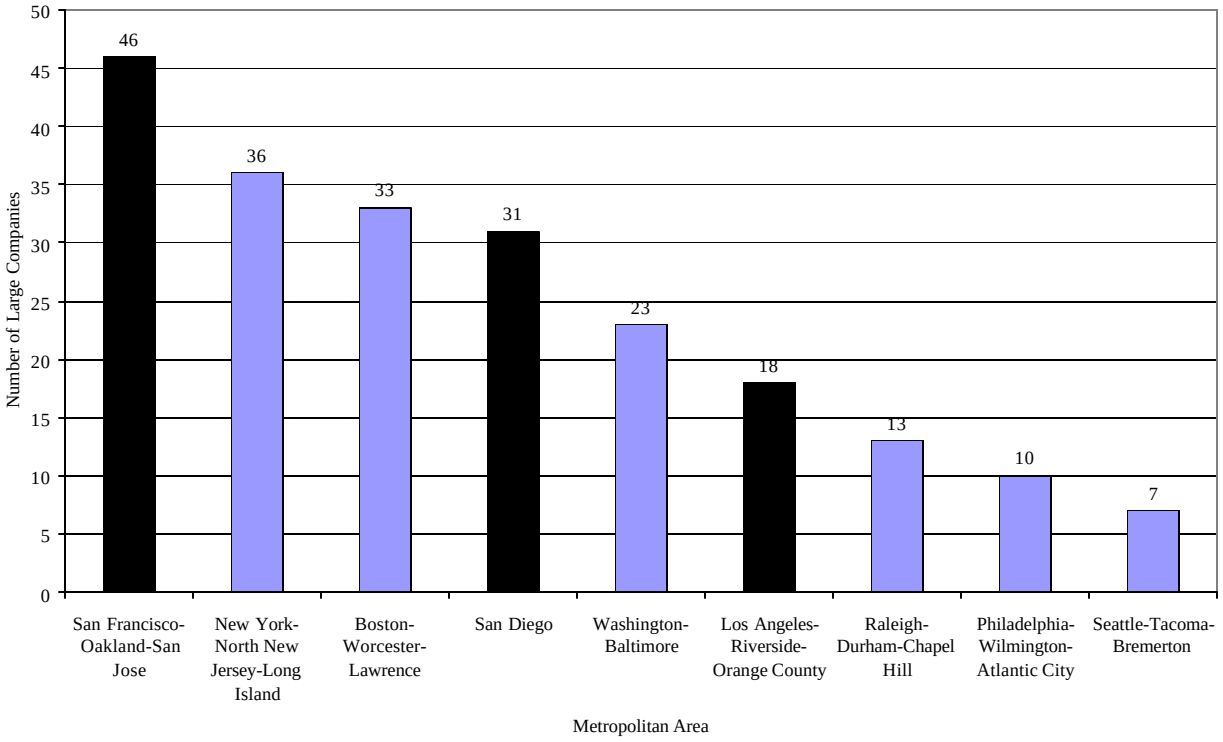
Clusters often grow up around prominent institutions or companies that are sometimes called "anchors." Universities and research institutions are vital anchors in the biosciences. They provide a region with name recognition and financial and educational resources. They spawn educated workers, scientific entrepreneurs, and a flow of ideas and inventions.

Clusters benefit from their region's concentration of inter-related companies and institutions. Equally important are the informal social networks that form in such an environment. Crucial transactions follow the lines of these informal relationships – for example, the formation of partnerships between scientific innovators and business entrepreneurs, or the linking of companies with venture capital.

Clusters can develop a critical mass that gives them an advantage over competing regions. As they grow in size and density, these very characteristics make them more appealing to entrepreneurs and investors making decisions about where to locate – a sort of snowball effect. By the same token, a region that lacks a critical mass of companies and supporting industries and institutions may have trouble attracting companies, investment, and talent.

The distribution of larger biotechnology companies gives a sense of where the biotechnology industry has matured.[80]

Figure 3
Regional Biotechnology Concentrations
As Measured by Number of Larger Companies (100+ Employees) *



Source: Brookings Institution 2002[81]

San Francisco Bay Area

The Bay Area's leadership in the bioscience industries is not surprising given the region's prominence in other kinds of technology – semiconductors, aerospace, personal computers, and the Internet. The Bay Area is arguably the birthplace of the biotechnology industry. Pioneering recombinant DNA experiments that laid the foundations for genetic engineering were performed at Stanford University. Genentech, the first company to market a biotechnology drug, was founded in South San Francisco in 1976.

* In compiling these numbers, the Brookings Institution defined biotechnology as "the application of biological knowledge and techniques pertaining to molecular, cellular, and genetic processes to develop products and services". Their geographic unit of analysis is the U.S. Census Bureau's Metropolitan Statistical Area (MSA).

The region is home to dozens of universities and nonprofit research centers. These include such leading bioscience institutions as UC Berkeley, UC San Francisco, and the U.S. Department of Energy's Joint Genomics Institute in Walnut Creek.

The Bay Area consistently attracts the largest share of California's biosciences venture capital.[82] It is also a magnet for federal dollars. For example, the region attracts more National Institutes of Health (NIH) grant money than any other region of the state.[83] Large pharmaceutical companies have been investing heavily in the region through joint ventures, alliances, and licensing and royalty arrangements with biotechnology firms.[84]

According to CHI, the Bay Area's biomedical industry employs 80,286 people in 713 companies.[85] According to another recent regional analysis, Bay Area bioscience companies account for 52,000 jobs. The area's academic and research institutions employ an additional 10,000 people working in the life sciences, according to one estimate.[86]

San Diego Region

The San Diego region was hit hard by the downsizing of the defense industry in the early 1990s, but the region's strong research infrastructure and its medical bioscience industries have helped it to rebound.[87]

According to the region's biotechnology industry association, the San Diego region's life sciences industry contains nearly 400 companies and research institutions. By their estimate, the region's employment in the life sciences grew by 250% from 1991-2001.[88] According to CHI, the San Diego "biomedical cluster" employs 29,491 people.[89]

The San Diego region boasts 18 universities or nonprofit research centers.[90] The San Diego life sciences industries are considered particularly strong in medical devices, biopharmaceuticals and agricultural biotechnology companies.[91]

Southern California Outside San Diego

There are numerous biotechnology companies throughout Los Angeles, Orange, Santa Barbara, Ventura, San Bernardino, and Riverside Counties. According to the Los Angeles Regional Technology Alliance (LARTA), there are 2,090 bioscience companies employing 64,700 people in these counties.[92*]

Southern California is also at the forefront of the emerging nanotechnology industry, with key discoveries coming out of UCLA, Caltech, and Southern California laboratories such as the NASA Jet Propulsion Laboratory.[93] The new state-funded California Nanosystems Institute is housed at Caltech and UC Santa Barbara.

[*] The biosciences, as defined by LARTA, involve "the study of living cells and materials to improve human health, animal health, agriculture and the environment."

Los Angeles and Orange Counties are the region's leading counties, with particular depth in medical devices and pharmaceuticals. Los Angeles County has, according to a recent LARTA study, 593 medical device companies and 158 pharmaceutical companies; Orange County has 350 medical device companies and 83 pharmaceutical companies.[94] The region also has a number of world-class research institutions, including UCLA, UC Irvine, Caltech, and numerous medical research institutions.[95]

Although the numbers are impressive, LARTA notes that the southern California region's bioscience industries are much more widely dispersed than in San Diego or the Bay Area. The region has "not fostered a critical mass of high-profile, large, and influential companies that might help brand the region as one of the world's finest … Southern California is fairly effective at building small and medium-sized bioscience companies, but…it fails to move companies to higher stages of growth."[96]

Sacramento, Yolo and Solano Counties

The proximity to Central Valley's agriculture industry and the University of California at Davis have helped to bring biotechnology to this area. For example, Calgene, the first company in the United States to market a genetically modified food (the "Flavr Savr" tomato) got its start in Davis.

The area has also benefited from the woes of the neighboring San Francisco Bay Area – in comparison to the Bay Area, land and housing are inexpensive, and traffic problems less severe. For example, inexpensive land helped convince Bay Area biotechnology pioneer Genentech to build a new pharmaceutical manufacturing plant in Vacaville (Solano County).

As yet, the region has not achieved anything like the prominence of the others highlighted above. The region has only an estimated 4,600 workers employed in the biomedical technology field (as compared to as many as 80,000 in the Bay Area). As the *Sacramento Bee* has noted, "Sacramento has been on the verge of a biotech boom for years, and the explosion still hasn't happened."[97]

Trends and Challenges for the Bioscience Industries

Many of California's political leaders consider the bioscience industries to be vital for California's future economic prosperity. In order to develop policies regarding the bioscience industries industry, it is helpful first to understand some of the major trends and challenges affecting its growth.

THE LONG ROAD TO REVENUES

As a form of business, the bioscience industries tend to be very capital-intensive. For innovative technologies, product development often involves both a great deal of research and development (R&D) and a demanding regulatory approval process. Particularly for young companies, this can mean a lengthy, expensive startup period, fraught with uncertainty, during which there are no revenues from the products being developed.

Research Before Revenues

A few statistics will illustrate how research-intensive the bioscience industries can be:

- California biomedical firms invest 45% of operating expenditures on R&D, according to a CHI survey.[98]
- Thirty-five percent of these companies reported earning no revenue in 2000, and 40% did not yet have products on the market.[99]
- In 2000, 60% of the firms surveyed by CHI expanded R&D spending within the state, and 68% expected to expand R&D in California within the next two years.[100]
- In comparison, the software industry invests an estimated 10-20% of revenues on research and development.[101] According to Standard & Poor's, the average industry invests about 4-5% of revenues in R&D.[102]

Challenges to Bring a New Invention to Market

After a medical device or biopharmaceutical company has completed its research and development, it will have to sponsor clinical trials to prove the product's efficacy and safety. Even after that, regulatory review adds to product development time. In 2001, the drugs approved by FDA took about 19 months to complete the regulatory process.[103] The regulatory process is less costly for medical devices than for pharmaceuticals. Demonstrating the effectiveness of a medical device requires less extensive clinical trials than is required for drugs.[104] As of FY 2001, average review time for pre-market approval (the full-blown FDA review process for medical devices) was 13-14 months from submission to decision.[105]

The biggest challenge for many companies during product development is the difficulty of securing venture capital for technologies that may be far away from the market.[106] For medical devices, this difficulty is compounded by the fact that the market for a new medical device is often smaller than for pharmaceuticals. The availability of venture

capital has been hurt by some unsuccessful stock offerings, particularly for smaller firms.[107]

For medical devices, another major issue is payment or reimbursement – acquiring approval from insurers to cover and reimburse for new medical devices can require several years of effort beyond FDA approval.[108] Manufacturers of medical devices complain of a lack of consistency, clarity, and timeliness in payment processes and their criteria in the federal Medicare program, the state's Medi-Cal, and the private managed care institutions. The problem is less for technologies that represent incremental changes, greater for innovative new technologies.[109]

A related challenge for medical device firms is the rising use of managed care and cost-limitation strategies among health insurers that tend to push patients toward pharmaceutical treatments rather than more costly surgical procedures using sophisticated medical devices. However, some medical devices, for example laser or laparoscopic surgical devices, have been very successful precisely because they can reduce treatment costs and hospital stays.[110]

The Transition to Manufacturing and Marketing

With the large number of biotechnology drugs in the development pipeline, a major question has arisen over how these companies will make the transition from R&D to commercial success. A biotechnology company that has invented a new drug often lacks the knowledge and facilities for manufacturing, marketing, and distributing it in commercial quantities. This requires financing and construction of costly facilities. Manufacturing must be conducted so as to pass rigorous government quality control standards.

One of the barriers to this transition could be the lack of manufacturing capacity in California. Biopharmaceutical manufacturing is a technically exacting, highly automated process that requires a very specialized type of facility as well as an array of skilled workers, technicians and scientists. Demand for the protein-based biotech drugs now on the market already outstrips the industry's production capacity. Companies that have made huge investments in developing drugs are at risk of losing much of the potential revenues because they can't manufacture enough of their product.[111]

This transition also requires a different set of management skills, and a larger workforce with skills not found in an R&D laboratory. If a company decides to expand, the timing is key. It could be disastrous if a company expands prematurely and then problems arise in the product development or regulatory process. Yet companies must be ready to manufacture to capitalize quickly on the product once it is approved and ready for the market.[112]

Bioscience Investment: A Boom And Bust Cycle

Because the product development cycle is so lengthy, bioscience firms can burn through a great deal of investment capital. For example, in 2000, U.S. biotechnology companies

raised investment capital of $32.7 billion, including stock offerings and venture capital. For comparison, annual revenues from product sales and other sources that year totaled $25 billion.[113]

However, despite the many grand predictions about the future of the biosciences, the attractiveness of bioscience firms to investors has always been volatile. Investors are often cautious about investing in an industry where the road to profits is so long. When the markets are cautious, investors favor companies that are further along in terms of revenue growth, making it harder for startups and earlier-stage companies.

Biotechnology in particular attracted a great deal of attention and investment from venture capitalists in the 1980s, but then the industry's fortunes sagged in the 1990s.[114] This corresponded in part to the ability of investors to realize quick profits elsewhere as information technology boomed.[115] Other factors included a series of high-profile product failures, and concerns that managed care cost-containment would drive down profits.[116] Similar issues caused the medical device industry to go through a wave of consolidation in the 1990s.[117]

The volatility in investor attitudes has been reflected in sharp swings year-to-year in the success of biotechnology stocks and stock offerings. In 2000, their best year ever, publicly traded medical biotechnology companies reaped $29.9 billion from stock and other equity investments. In 2001, the total was down to $5.5 billion.[118] This year the Wall Street Journal noted that the downturn in biotechnology stocks made it "all but impossible for cash-hungry biotech firms to raise money in the stock market" and raised concerns that some smaller companies would "burn through" their available cash.[119]

California does well relative to other states in the quest for capital. According to CHI, 45% of total U.S. biomedical venture capital went to California companies in 2000.[120] California also leads the nation in capital raised through initial public offerings.[121]

Progress and Setbacks in Gene Therapy

Thousands of labs throughout the world are working on gene therapy. Federal funding has been growing, and numerous trials are ongoing, most of them involving new cancer treatments or vaccines. Gene therapy has yet to become a major commercial force. The great majority of clinical trials are still in early phases, and many of them are funded by the federal government, academic institutions, or foundations.[122]

There are high hopes for gene therapy to make major contributions to medicine, but the road has not been smooth. Gene therapy's backers were disappointed when a patient died in clinical trials in 1999. Hopes rose again this year with the announcement of a major success – the successful treatment of children born with severe combined immunodeficiency (the so-called "bubble boy disease").[123] However, it was soon discovered that one of those patients also contracted a leukemia-like illness that may have been caused by the gene therapy.[124]

OPTIMISM IN MANY SECTORS OF THE BIOSCIENCE INDUSTRIES

Employment growth in California's biomedical industry during the last decade was steady if unspectacular – 21% according to one estimate.[125] This was comparable to the pace of the overall growth of the state's labor force during the same period. However, there are a number of reasons observers are optimistic about the potential for strong growth in the biosciences in the future.

According to Standard & Poor's, the advanced medical device industry is in a strong position to grow rapidly in coming years: "technological breakthroughs are coming just ahead of an expected baby boomer-driven surge in demand … Expanding amounts of research have generated growing pipelines of significant new products."[126]

Similarly, a large number of new biopharmaceuticals are now in development or nearing commercialization. According to the Biotechnology Industry Organization, as of 2001 there were more than 350 biotech drug products and vaccines in clinical trials targeting more than 200 diseases.[127] Ernst & Young estimates that as many as 240 new medicines could reach the market by 2007.[128]

The worldwide medical device market grew an estimated 10% from 2000 to 2001, according to Standard & Poor's.[129] Nationwide revenues of medical biotech companies have increased by an average 11% per year since 1995, according to Ernst & Young.[130]

Integration of the Biotechnology and Pharmaceutical Industries

In making the difficult transition from research shop to profitable enterprise, many biotechnology companies are tapping the resources of large pharmaceutical companies. A few biotechnology companies are trying to become pharmaceutical companies in their own right, manufacturing and marketing their products.

Many biotechnology companies form alliances or partnerships with pharmaceutical companies, or are purchased by them. Pharmaceutical companies are hungry for innovative ways to find new products. According to one recent estimate, pharmaceutical companies typically spend $800 million to develop new drugs (including both R&D and the regulatory process).[131] Biotechnology may offer cheaper ways to develop drugs.[132]

Another reason the large pharmaceutical companies are hungry for the discoveries of biotechnology firms is that the patents on many profitable drugs are expiring.[133] Despite large investments in R&D by pharmaceutical companies, "the rate at which new drugs reach the market has declined over the past 15 years. That rate is now well short of what is needed to sustain the sector."[134]

A major question now is to what extent biotechnology companies will simply function as R&D adjuncts to the established pharmaceutical companies, or whether many of them will rise up as direct competitors (a few have already done so). By the mid-1990s, medical biotechnology companies were tending to specialize in a research area and outsource other functions, such as clinical trials, manufacturing or marketing. They

increasingly entered partnerships, joint ventures, or other alliances with pharmaceutical companies or larger biotech companies, offering to share the marketing rights to their discoveries.[135] Such deals often require the biotechnology company to give up a hefty share of their rights to profit from their inventions (or even allow themselves to be absorbed entirely).

Not all bioscience firms want to rely on large pharmaceutical companies for their manufacturing. According to a CHI survey, in the year 2000, 52% of California bioscience firms expanded manufacturing. Sixty-eight percent expected to expand manufacturing within the next two years.[136]

Biopharmaceutical manufacturing could be a major area of opportunity for job and wealth creation in the state. While California is by far the nation's leader in spawning innovative biotechnology startup companies, these enterprises don't become lucrative until their products are commercialized and manufactured. In the past, the major bastions of pharmaceutical manufacturing have been on the East Coast. Yet many of their facilities are aging, and biopharmaceutical manufacturing demands a new kind of facility where production and quality control is more automated. California will reap far greater rewards from biotechnology if it can become the favored locale for this new generation of manufacturing facilities.[137]

Human Genome Mapping

The federally-funded Human Genome Project and related private efforts have made great strides in mapping the sequences of human DNA. At the same time, these advances are spawning new fields of research as scientists work to identify the functional genes in these sequences, and to understand the proteins produced by these genes. Ultimately, the complex interactions between these genes and proteins govern much of the structure and function of the human organism. Among biotechnology companies, a gold rush mentality has set in as companies scramble to identify human genes, and patent related medical discoveries.[138]

Bioscience Meets Information Technology

High-speed computers using tools such as statistical and database software and graphical simulation are being increasingly used in medical research. At the same time, new automated techniques known as high-throughput screening and combinatorial chemistry are used to rapidly test and analyze large numbers of compounds, cells, or DNA samples.

The convergence of biology and information technology is prompting technology companies such as IBM, Compaq and Sun Microsystems to enter the biomedical field. It is also leading to new partnerships between different kinds of companies.[139] So far, however, the growth of the bioinformatics field has reportedly been slower than expected, in part due to a lack of standardization and integration among the various computing platforms and software systems coming into use.[140]

Industrial and Environmental Biotechnology

Industrial and environmental applications of biotechnology are still largely in the early, formative stages. Although it is still a small part of the biotechnology business, there are signs of the growing importance of this sector. Industrial biotechnology startup companies are growing more numerous. Venture capital firms are beginning to dedicate funds to them. There is increasing interest in funding such research at the federal level, due to the potential payoffs in industrial sustainability, energy efficiency, and reduced reliance on fossil fuels. Most of the major chemical companies are also investing in or forming partnerships with biotechnology companies.[141]

Nanotechnology Coming Into Its Own

Nanotechnology could revolutionize the entire medical technology field. Such a revolution, if it comes, is probably decades away. Nevertheless, nanotechnology is beginning to emerge as an industry, not just a field of basic research.

Despite the fact that nanotechnology is still young, the state and federal governments are betting heavily on its future. The federal government has proposed over $500 million in nanotechnology research funding for 2002.[142] In 2000, Governor Davis and the California Legislature launched the California Nanosystems Institute, pledging to invest $100 million in the public-private partnership.[143]

THE TRAVAILS OF AGRICULTURAL BIOTECHNOLOGY

Despite the predictions of a new "green revolution," agricultural biotechnology has gotten a slow start in comparison to medical biotechnology. Only a few types of transgenic crops are in wide use. Surprisingly, in California, the nation's leading agricultural state, biotechnology has been particularly slow to take root. There is presently little acreage planted with genetically modified crops of any kind in this state.

Two of the most widely used transgenic crops in the U.S. – corn and soybeans – are not grown in large amounts in California. There are, however, a number of already-approved biotechnology crops that could be grown commercially in California, such as herbicide-tolerant lettuce, virus-resistant squash, and various kinds of GM tomatoes.[144] About thirty varieties of biotech crops have been developed and field tested by California companies.[145] Why isn't there more commercialization of transgenic crops in California?

Costs Versus Benefits in California Agriculture

It can be costly to develop a new biotechnology crop and shepherd it through the regulatory system. One factor driving up the costs is the proliferation of patents and property rights controlling the use of genetic sequences and genetic engineering techniques. For example, the "Golden Rice" designed to cure vitamin A deficiencies in developing nations incorporates technology based on at least 70 patents with 32 owners.[146]

The costs of R&D and complying with the federal regulatory process are substantial for agricultural biotechnology (although not in the same league as the costs associated with drug development). Estimates of the cost of developing a new crop range from a half million dollars to $10-15 million or more, depending on how novel and complex the engineered traits are.[147]

Costs are probably one reason that the market has so far favored biotech crops that are grown on a very large scale (corn, soybeans, and cotton).[148] The economics are less favorable for California, which grows a great number of small, high-value crops rather than a few large-acreage crops.

However, in California and worldwide, the main impediment to the industry seems to be uncertainty about the market in the face of the controversies that have surrounded genetically modified food. The incentives to develop and market new crops often are not sufficient to overcome the doubts.

Agricultural Biotechnology Dogged By Controversy and Market Fears

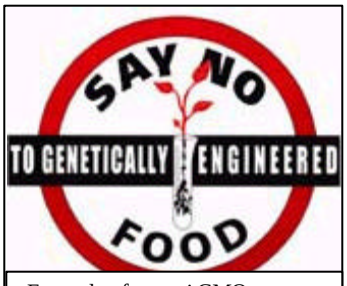
There are several inter-related factors contributing to this uncertain market:

- The reaction abroad
- Consumer attitudes in the United States
- Anti-GM food activism by advocacy groups
- Doubts about the regulatory system
- Resulting caution in the food production and marketing industries

The Reaction Abroad

The reaction to genetically modified foods has been much more hostile in Europe and many other countries than it has been in the United States. In Europe, the reaction has been attributed to factors ranging from the influence of Green political parties to fears over a series of food safety crises, including mad cow disease.

Europe requires the labeling of GM food imports, and has not approved any new GM foods for several years.[149] The restrictions are estimated to have cost U.S. corn exporters an estimated $200 million annually since 1998.[150] U.S. farmers have avoided a number of new biotechnology seeds to prevent similar losses.[151]



Example of an anti-GMO campaign logo.

Right or wrong, the U.S. position against labeling transgenic food is somewhat out of step with the rest of the world. The U.S. is not among the over 100 countries, including the European Community and Japan, that have signed the Cartagena Protocol on Biosafety of 2000.* Signatories agree to label shipments that may contain

* As of this writing 36 countries had ratified the Protocol.

bioengineered commodities, and allows countries to block imports of GMOs in the absence of sufficient evidence about their safety.[152] Europe is now preparing to tighten its labeling and tracking requirements for GM food ingredients. Compliance costs and reduced sales could cost U.S. exporters billions of dollars. U.S. officials fear the new rules could become a model for other countries throughout the world.[153]

Some recent developments suggest resistance abroad could eventually soften. For example, last summer, the United Nations World Food Summit gave a cautiously-worded endorsement to biotechnology as an avenue for alleviating world hunger.[154]

Consumer Attitudes in the United States

Public opinion polls show that concern about GM foods is widespread among U.S. consumers. However, there is also a good deal of ambivalence. Some of the most noteworthy points revealed in such surveys:

- A bare majority are in favor of genetically modified foods, although a majority oppose genetic engineering of animals.
- Most consumers say they favor labeling of genetically modified products.
- Consumers are often fairly ignorant about biotechnology, which implies that their opinions might still be shaped by new information.
- Biotechnology is not the most important food safety issue for consumers.

According to a recent survey conducted at Rutgers University, fifty-eight percent of consumers said that they approve of using genetic modification techniques to produce new plants, and 37 percent disapprove. Only 28 percent approved of using these techniques to produce new animals. Ninety percent said that GM foods should have special labels on them, and 48 percent said that they would not buy fresh vegetables if they were labeled as produced through genetic modification.[155]

According to the Rutgers study, only about 40% of consumers know that GM products are being sold at grocery stores. Ignorance and misconceptions were common (for example, nearly half believed the statement that "ordinary tomatoes do not contain genes, while genetically modified ones do").

Another poll, conducted in 2001, found that consumer opinion is still forming and may be fairly malleable. When consumers were told that at least half the products on grocery store shelves already contained GM ingredients, one out of five who had said they were unsafe changed their minds and concluded they were safe.[156] Furthermore, numerous surveys have indicated that other issues are still more important to consumers, such as food freshness, pesticides, or foodborne diseases.[157]

The food industry is concerned that the current biotechnology crops offer benefits mainly to agricultural seed companies (increased market share), and to farmers (increased yields,

reduced costs) but not to consumers.* Thus, those marketing food products are left to deal with the negative publicity generated by GM food controversies without any tangible offsetting benefits to offer to consumers.

Some argue that a stronger regulatory system and food labeling could have reassured consumers that these novel products were safe and beneficial. Jeremy Rifkin, one of the leaders of the anti-GMO movement, says that the industry's aversion to FDA-mandated safety testing and labeling helped galvanize his movement. Some industry leaders agree. Roger Salquist, formerly the CEO of Calgene, the company that brought the Flavr Savr tomato to market, was recently quoted as saying, "How could you argue against labeling? … The public trust has not been nurtured."[158]

Anti-GM Food Activism

Boycotts and protests against some companies have caused others to become reluctant to allow themselves to be so closely identified with GM crops. For example, baby food makers Novartis (the maker of Gerber products), H.J. Heinz Co. of Pittsburgh and California-based Healthy Time Natural Foods, have pledged to remove or avoid genetically modified ingredients in response to pressure from the environmental organization Greenpeace.[159] Food companies like Frito-Lay, and grain companies like Archer Daniels Midland and Cargill have asked farmers to separate genetically modified foods from traditional ones.[160] Some products, such as Odwalla beverages, carry labels boasting they are GMO-free.

More recently, Greenpeace has suggested that if California winemakers use genetic engineering to combat Pierce's Disease, they may face rejection or boycotts by consumers in other countries.[161†] Anti-GM activists are busy on a number of other fronts, including protests and letter-writing campaigns directed at Kraft, Safeway, and American corn growers.[162]

Doubts About the Regulatory System and the StarLink Episode

StarLink was a pest-protected (Bt) corn plant developed by AgrEvo, now a subsidiary of Aventis. Pre-market tests had shown that the form of Bt pesticide produced in StarLink plants was a possible food allergen because it was not readily broken down in the human digestive tract. The U.S. EPA approved StarLink with the provision that it be kept out of the human food supply and used only for animal feed and ethanol manufacture. Farmers were to be informed of the restrictions and were supposed to sign an agreement not to sell StarLink for human consumption.[163]

* Biotechnology proponents point out that some of these products can offer benefits to consumers as well as farmers – for example, they arguably reduce the price of agricultural products, prevent pest damage to food, and may reduce the use of more harmful pesticides or herbicides. However, these benefits would not likely be very apparent to consumers.

† Pierce's disease is an insect-borne plant disease that threatens California's wine industry. Many experts believe biotechnology could be one of the most promising avenues for defeating this threat.

In the summer of 2000, a coalition of environmental and consumer groups released test results showing that StarLink corn had found its way into taco shells made by Kraft Foods. These disclosures created havoc in the corn industry, requiring massive recalls, undermining consumer confidence, and severely harming export markets.[164] The ripples from the StarLink debacle continue to be felt worldwide, as the tainted corn was found in numerous corn products, and in corn shipments to Japan, the largest foreign market. Japanese corn imports dropped dramatically. South Korea, the second-largest importer of U.S. corn, banned it entirely.[165]

The impact of the StarLink episode was evident in a 2001 news media study showing that comments in the media about possible negative health consequences of food biotechnology outpaced claims about the technology's benefits by a margin of eight to one.[166]

StarLink also added support to the passage of the California Rice Certification Act of 2000. The bill was backed by the California Rice Commission, a trade group representing growers and millers, who were reportedly worried about the potential loss of export markets if genetically altered rice was accidentally mixed in a shipment to a country such as Japan where anti-GM sentiment runs strong. Opponents, including biotech companies, said that the new system will needlessly stigmatize GM rice, not to mention adding to its cost by levying a fee on it.[167]

POTENTIAL PROBLEMS WITH CALIFORNIA'S BUSINESS CLIMATE

California bioscience companies report that they face an additional set of challenges that impact the cost and desirability of doing business in this state. These include infrastructure, land and housing costs, the quality of life, and the quality of the workforce.

Infrastructure, Land, Housing, and Quality of Life

By 1995, the Bay Area had gained the distinction of becoming the most expensive region to live in the entire United States.[168] Rising housing costs, traffic congestion, and under-performing public schools compromised living standards for many Silicon Valley residents even as the region enjoyed the 1990s technology boom.

In San Diego, the bioscience industries similarly view housing prices as a key issue affecting their future growth.[169] In much of Southern California, bioscience companies are finding space for laboratory and industrial expansion is in short supply.[170] A recent study by the San Diego Regional Economic Development Corporation found a potential shortage of space zoned industrial in the region.[171] Much of the currently zoned industrial land is undevelopable due to terrain or other impediments.[172]

As the cost of living escalates, the strength of the workforce can be eroded. California has a skilled and educated workforce, particularly in the regions with significant bioscience industry clusters. However, there are signs that California is falling short in producing enough qualified employees, researchers, and managers for bioscience companies. This was a prominent theme in testimony from biotechnology and medical

device executives in hearings last year before the California Assembly Select Committee on Biotechnology.[173]

According to one estimate, it takes California biotechnology companies 14-16 months to recruit a candidate in some critical positions. California biotechnology companies are also worried about wage escalation as the cost of living rises.[174]

Aside from the quality of life issues, number of other factors contribute to the workforce problem.

Changing Labor Market

Educational institutions and other workforce training programs often find it difficult to keep up with industries founded on rapidly evolving technology businesses. Faculty members may be unaware of the skills currently needed in the workplace. Furthermore, publicly funded universities are under pressure not to add new requirements that increase the already lengthy average time it takes students to complete a degree.[175]

For example, as the biopharmaceutical industry matures, the needed skill sets to run a sophisticated biopharmaceutical manufacturing plant are not readily acquired in many colleges or in other industries.[176]

The bioscience labor market can also be volatile. For example, industry analysts Ernst & Young said in 2001 that the convergence of biotechnology and computing should keep demand high for professionals with information technology skills.[177] However, a year later, with the IT industry slump showing no signs of abating, high-level computer jobs in the biosciences were proving scarce.[178]

Foreign Workers

One indication of California's capacity to fill bioscience positions is the number of foreign workers brought in to fill technology jobs through the H-1B visa program.* According to recent surveys conducted for the industry, about 9% of California's biotechnology workforce is composed of foreign H-1B visa holders. According to this study, their skills are "either largely unavailable in the general U.S. labor pool or are in high-demand areas which California higher education currently cannot provide due to the paucity of key training programs and inadequate resources…"[179]

Problems in the Educational System

The California Council on Science and Technology recently published an extensive study of the shortfalls in California's science and technology educational system. According to the study, students in California's K-12 schools are not sufficiently interested or aware of science and technology career paths. Furthermore, not enough of California's K-12

* Foreign workers with skills not available in the domestic labor pool can gain these visas to stay in the U.S. for up to six years, after which they can apply for permanent resident status.

graduates are sufficiently trained to attend college, particularly in science and mathematics.[180]

The problems in the K-12 and community college systems contribute to the shortage of science and technology graduates with four-year degrees, the minimum qualification for many high-tech jobs. CCST also noted that the community colleges lack sufficient resources and facilities for science education and are not producing enough science and engineering graduates to meet the state's technology workforce needs.[181]

Changing demographics will likely increase the importance of the traditional shortfall in female and minority enrollment in science courses. In the future, the majority of the state's citizens will belong to ethnicities – African American, Latino, Native American – that are underrepresented in science and engineering fields.[182]

Regulations and the Cost of Doing Business

Local officials and industry representatives note that California must often compete with other states to attract and retain bioscience businesses. State laws and regulations can add additional costs into the equation when companies decide where to locate or expand. These can range from laws on worker's compensation to environmental laws such as the California Environmental Quality Act and stormwater permits.[183] Some in the industry and local government feel that California's regulatory climate makes it more difficult for bioscience companies to locate or remain in California.

Technology Transfer: Problems at Intersection of Industry and Academia

Technology transfer occurs when ideas developed in academia make their way into the commercial marketplace. This helps bring innovations into the industry and can also provide lucrative licensing fees for the university.

According to some critics, the technology transfer process in California's universities sometimes "moves at a snail's pace through the government systems as well as the university systems," which are "clogged with the veto power of too many people, paperwork and politics."[184] Some private companies complain that the University of California technology offices remain slow-moving or uncooperative, and that they sometimes place unreasonable demands on companies wishing to collaborate.[185]

The University of California has recently taken a number of steps to reform its technology transfer system, the results of an internal review that commenced nearly a decade ago. These reforms are designed to make the University's research relationships with outside parties more flexible and decentralized.[186]

In addition, individual UC campuses such as San Diego, Berkeley, and Irvine have initiated reviews of their own technology transfer policies and operations.

Technology transfer and university-industry collaboration can be controversial because of concerns about the differing goals and missions of academia and the private sector.

Critics raise concerns such as potential conflict of interest, the tension between academic openness and commercial confidentiality, and the influence of corporate interests on university research priorities. Yet such arrangements also help to fund university programs, research, and graduate students.

Government Support for the Bioscience Industries

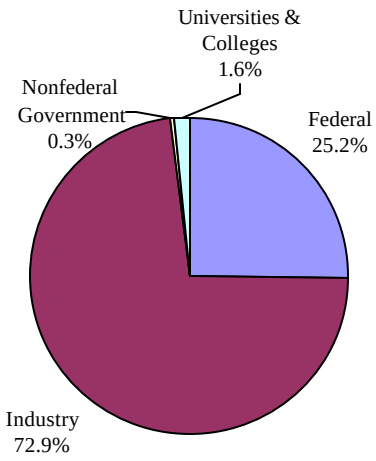
Before exploring policy options for the bioscience industries, it is necessary to outline the existing government policies. We will deal first with programs to help the bioscience industries, then discuss regulation.

Programs that assist the bioscience industries include subsidies, tax incentives, and the funding of educational and research institutions. Some of these programs are targeted directly at the bioscience industries, while others spread their benefits more widely.

FEDERAL FUNDING OF RESEARCH AND DEVELOPMENT

Private industry is the largest funder and performer of research and development in the state. In 1998, the last year for which National Science Foundation figures are available, private industry funded 73% of the $43.9 billion in R&D performed in the state. However, the federal government also made a major contribution, funding over 25% of the total.

Figure 4
R&D Funding Sources in California, 1998



Source: National Science Foundation 2000

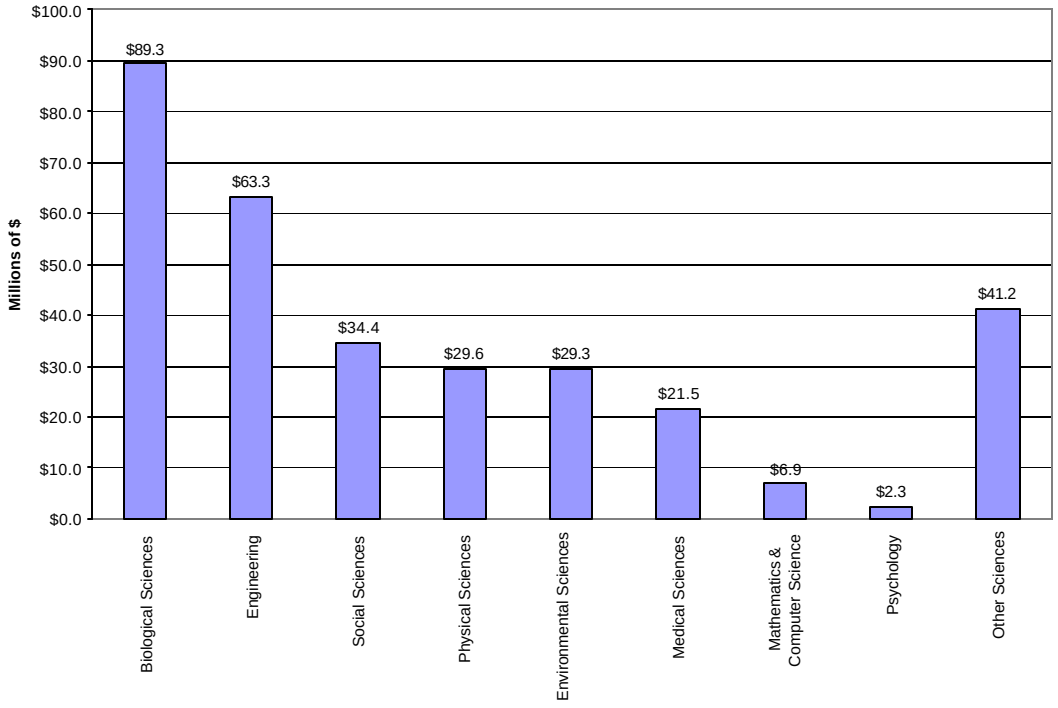
The UC system is a large beneficiary of federal funding. In 2000-2001, the UC system expended $2.3 billion on research, of which 52% was federally funded and 19% was state funded.[187]

The largest source of federal funding for the biosciences is the National Institutes of Health (NIH). In FY 2001, California received $2.5 billion from NIH in grants for research, training, fellowships, and R&D.[188]

STATE FUNDING AND INCENTIVES

The state of California also spends hundreds of millions of dollars supporting research and development in a variety of fields, including the biosciences. Recent data on patterns of state expenditures for R&D are not readily available. However, according to a California Council on Science and Technology (CCST) estimate, California spent $317.8 million on R&D in FY 1995-1996, including $274 million in state funding and $35 million in state expenditures of federal funds. Most of the funding went to academic institutions, and biological sciences and medicine received the largest share (about 35%). About 71% of the state funding came from direct appropriations.[189] The breakdown of spending is shown in Figure 5 below.

Figure 5
1995-1996 California Funding of R&D, By Field



Source: California Council on Science and Technology 1999[190]

The total state research funding has gone up since then. In FY 2000-2001, the University of California expended $455 million in state funds on research.[191]

CALIFORNIA'S PUBLICLY FUNDED COLLEGES AND UNIVERSITIES

The state's publicly-funded colleges and universities – the University of California, the California State Universities, and the community colleges – are cornerstones of the state's bioscience industries. Their research advances the underlying science, their

discoveries lead to new products, and their faculty and graduates become the staff and management of private companies. Taken together, in 1999-2000 the UC and California State University systems awarded 6,859 bachelors degrees in the biological sciences, as well as 426 masters degrees and 315 doctorates.[192]

A survey conducted by UC researchers documented the close linkages between the University of California and the biotechnology industry:*

- One in three publicly traded biotech firms in the United States is located within 35 miles of a UC campus
- 85% of California biotech firms employ UC alumni with graduate degrees
- 1 in 4 California biotech firms were started by UC scientists, including some of the largest.[193]

There are many forms of collaboration between the University of California and the bioscience industries. Perhaps the most ambitious is the 2000 launching of four California Institutes for Science and Innovation. These Institutes are supposed to bring academia and the private sector together in order to expand commercial opportunities for California industries, strengthen their competitiveness in worldwide markets and stimulate the creation of new markets.[194]

One of the four centers will be the California Institute for Bioengineering, Biotechnology & Quantitative Biomedical Research, also known as QB3. It will be centered at UC San Francisco, UC Berkeley, and UC Santa Cruz. Another of these institutes, the California Nanosystems Institute, will also likely contribute to the biosciences. The state intends to invest $100 million in each center, and plans to leverage this with matching funds from industry sources.[195]

A related initiative is the new 43 acre, $1.4 billion satellite campus of UCSF at Mission Bay now under development. The Mission Bay campus is intended to become "the premier biomedical research and teaching center in the United States," and the afore-mentioned "QB3" biosciences institute will be among its tenants.[196]

There are numerous examples of academic-industry collaboration within the UC system, including:

- A five-year collaborative research agreement signed in 1998 between UC Berkeley and the Swiss pharmaceutical and agrochemical company Novartis.
- UC Davis is home to the University of California Life Sciences Informatics program, in which biomedical companies and the University of California co-sponsor research into the use of information technologies in the life sciences.
- UC San Diego's CONNECT is a center that links high-technology and life science entrepreneurs with resources such as management training and venture capital.

* The study surveyed 228 biotechnology companies, and got a 58% response rate.

The UC and CSU systems also have grant programs to encourage such collaboration. BioSTAR is a matching grant program in which biotech companies co-sponsor research projects at UC. The UC Systemwide Biotechnology Research & Education Program operates a biotechnology training grant program. The program funds combined research and training in science or engineering related biotechnology.

The California State University collaborates with industry through the California State University Program for Education and Research in Biotechnology (CSUPERB). CSUPERB's mission includes workforce development; technology transfer from the university to the marketplace; joint research with industry; and promoting the development of industry-oriented bioscience graduate programs. CSUPERB administers several grant programs to support student and faculty research and university-industry collaboration.

The California Community Colleges' economic development program, EDNet, administers the Biotechnology Initiative, a workforce development program. The program has six regional biotechnology centers throughout the state that administer job placement and student internship programs and developing model core curricula and academic support programs for industry. As of 2001, there were 30 community colleges (out of 108) with some biotechnology courses or a biotechnology program.[197]

WORKFORCE TRAINING PROGRAMS

In addition to its publicly funded higher education system, California has a number of programs intended to help train or re-train workers. For example, the California Employment Training Panel program awards grants to companies for worker training. The state's Manufacturing Technology Program provides small and medium-sized manufacturers with access to business assistance including workforce training.

There have been ongoing efforts to provide better coordination of California's highly varied and sometimes fragmented workforce training programs. In 1997, the Legislature ordered top state officials from several agencies* to form a partnership and develop a California Integrated Workforce Development Plan, which was issued in 2000. In 1999, in response to a restructuring of federal workforce programs, Governor Gray Davis established the California Workforce Investment Board (CWIB) to advise and assist in planning, coordinating, streamlining and monitoring California's workforce development programs and services. Since then, the state has been trying to restructure these programs around hundreds of "one-stop" service centers.

* The Secretary of Health and Human Services, the Secretary of Trade and Commerce, the State Superintendent of Public Instruction, and the Chancellor of the California Community Colleges.

OTHER PROGRAMS

There are several other state programs and initiatives that benefit the bioscience industries. Some are specifically targeted at the bioscience industries, while others are intended to promote high technology industries in general.

California Technology, Trade and Commerce Agency

The mandate of the California Trade and Commerce Agency's Division of Science, Technology and Innovation is to identify science and technology trends, help businesses and researchers to obtain R&D funding and early-stage capital, and coordinate the state's science and technology policies and programs. The Division administers several grant programs and provides technical assistance to high technology industries, including the bioscience industries. The Division is beginning to work with regional economic officials and business leaders to begin developing a bioscience strategy for the San Francisco Bay Area.

CalPERS California Biotechnology Investment Strategy

Believing that biotech is an "underfunded and undervalued industry," California's Public Employees' Retirement System (CalPERS) plans to invest $500 million in a portfolio of biotech companies with a variety of business models.[198]

Regional Technology Alliances

The Regional Technology Alliances (RTAs) are nonprofit public-private partnerships funded by the Technology, Trade and Commerce Agency and non-state matching funds. The program began as a defense conversion initiative, with three RTAs serving Los Angeles, San Diego, and the Bay Area. Three new RTAs have recently been added, serving the Inland Empire, Sacramento/Capital, and San Joaquin Valley regions.

The RTAs help administer a matching grant program for federally funded projects that accelerate the commercialization of new technologies. The RTAs provide technology businesses with a number of additional services, including consulting and information services, market studies, and workforce development initiatives.

Bio-Link (NSF)

Bio-Link is a nationwide program founded by the National Science Foundation, created to improve and expand educational programs that prepare skilled technicians to work in high technology fields. Bio-Link centers focused on biotechnology are located in San Francisco and San Diego. Bio-Link provides professional development for instructors, assistance with curricula, technology, and the sharing of information.

Technology in the High Schools

In 1997, the Legislature created the Digital High School Education Technology Grant Program (AB 64, Baca). Since 1998, the program has provided funding to help schools purchase wiring, hardware, curricula, and teacher training for teaching technology skills. A recent statute, AB 620 (Wayne, 2001) will provide grants to help establish ten high tech high schools with rigorous college preparatory programs in the sciences, mathematics and engineering.[199]

STATE AND FEDERAL TAX INCENTIVES

The state and federal governments support the bioscience industries indirectly through a variety of tax incentives. Many economists believe that private companies responding only to the market will under-fund R&D relative to its social and economic benefits.[200] Tax incentives are also justified as a way of supporting the growth of key segments of the economy such as small businesses or manufacturing. At the state level, tax incentives are often justified in terms of the need to compete with other states that are trying to lure businesses with their own tax benefits.

These incentives are usually not specifically targeted at the bioscience industries, and benefit many other types of enterprise as well.

R&D and Related Tax Credits

The federal government provides a Research and Experimentation tax credit amounting to 20% of incremental increases in R&D spending based on a four-year base period. Another important incentive for the bioscience industries is the orphan drug tax credit. It provides a 50% credit for testing expenses for developing drugs for rare diseases.

The State of California also has an R&D tax credit.[201] The credit equals 15 % of qualified R&D expenditures and 24% of basic research expenditures. The credit is based on the increase in R&D expenditures over a base period. Unused credits may be carried forward until they are fully used. Basic research must be carried out by qualified research institutions, such as medical organizations and research hospitals.

Accelerated Depreciation

California law allows deduction or rapid amortization of certain capital expenditures related to research, development, and experimentation.[202] This and the R&D credit cannot be claimed for the same expenditures.

Manufacturers' Investment Credit

This California credit amounts to six percent of qualified costs of personal property and equipment property that is purchased by manufacturing industries.[203] It applies to tangible personal property and capitalized labor used at least 50% in manufacturing, processing, refining, fabricating, or recycling. Unused credits may be carried forward for

seven years. For certain biotechnology companies and small businesses, the carry forward is 2 years longer, and there are also special provisions broadening the qualified property for biotech and biopharmaceutical companies to include buildings constructed for manufacturing, research, or storage.[204]

Net Operating Loss (NOL) Carry Forward

A portion of the state and federal deductions for operating losses from business activities can be carried over into subsequent tax years for up to ten years.[205] The percentage carryover for California tax purposes is currently 60%, and, under recently enacted legislation (AB 2065, Oropeza, 2002) increases to 100% in 2004. Certain businesses, including some biopharmaceutical or biotechnology companies, are already entitled to a 100% NOL carry forward.* There are currently $75 billion in unclaimed NOLs on the books.[206]

Federal law allows taxpayers to carry the full amount of a NOL back to each of the preceding two taxable years and forward to the succeeding 20 taxable years. There is no carry back provision for California's NOL deduction.

Manufacturers' Investment Exemption

State law exempts purchases of certain personal property by manufacturing businesses from the 5% state portion of the Sales and Use Tax (SUT). The qualifications are the same as for the Manufacturers' Investment Credit. The exemption is designed to help startups that may not have sufficient tax liability to benefit from other incentives. The sales tax exemption can also apply to the raw materials that are the components of medicines used in United States Federal Drug Administration (USFDA) clinical trials.[207]

Economic Revitalization Manufacturing Property Tax Rebates

Local governments can provide qualifying manufacturers with a rebate of some or all of their property tax for a period of five fiscal years from the date the property was placed in service. Qualifying property must be directly involved in the manufacturing process, lead to the creation of 10 new full-time manufacturing jobs, pay $10 per hour and those jobs must be in continuous existence for the duration of the rebate.[208] This law sunsets on January 1, 2003 unless extended by the Legislature.

Capital Investment Incentive Program (CIIP)

Another form of property tax rebate, this program allows cities and counties to cap the assessed value of any new manufacturing plant at $150 million for up to 15 years. The local government would then charge the manufacturer an annual "community services fee" equal to 25% of the value of the rebate.[209]

* The higher rate applies to "new businesses," and the term "new business" is defined to include any taxpayer that is engaged in biopharmaceutical activities or other biotechnology activities that are described in Codes 2833 to 2836 of the Standard Industrial Classification (SIC) Manual.

LOCAL GOVERNMENT INITIATIVES FOR THE BIOSCIENCE INDUSTRIES

Local governments throughout California and the country are trying to make their communities attractive to bioscience companies. For example, the City of Oceanside recently went to great lengths to become the site of San Diego-based IDEC Pharmaceuticals' new $1.3 billion pharmaceutical manufacturing facility. The new IDEC plant could bring 2000 jobs to Oceanside.[210]

The state provided training grants of about $450,000 for IDEC, but the lion's share of the incentives were local. Oceanside waived all of the local water supply and road impact fees for the project, a subsidy of about $1.5 million. In addition, the city is providing a five-year rebate of its share of the company's property taxes.[211] Some local officials feel the state is not doing enough to help them offer incentives to bioscience companies.

Last year the San Diego County Board of Supervisors adopted a Biotechnology Action Plan. Representatives of the industry and the county are working together on developing legislative policies to assist the industry. They are looking at issues such as workforce training, regulatory streamlining, and zoning changes to make land more readily available.[212]

The regions with strong bioscience industries tend to have dense clusters of related companies. Hence, many locales are investing in the development of biotech corridors or campus-style research parks that will contain bioscience companies and facilities. In Southern California, these communities include Pasadena, Los Angeles, Irvine, and San Pedro.[213] In San Diego, the biotechnology industry association BIOCOM has proposed a regional park of about 1,000 acres in San Diego County. Land and improvements for such a regional technology park could cost $175-220 million.[214]

In Northern California, efforts are underway to establish a Contra Costa Bioscience Incubator. The range of features and services planned is ambitious: wet lab space and equipment; furnished office space with flexible leases; assistance in regulatory compliance and product commercialization; networking with financial institutions and venture capital; accounting and legal services; and educational programs including seminars and conferences. The incubator would be a nonprofit corporation funded by public investment, private sector sponsors, grants, and fees paid by tenants.[215]

ARE STATE INCENTIVES AND SUBSIDIES GOOD PUBLIC POLICY?

It should be noted that directing subsidies or tax incentives toward a particular industry or industrial sector raises questions about whether such programs represent good policy-making, as opposed to simply providing benefits for a special interest group.

The Effectiveness of Tax Incentives

Tax incentives do cost the state lost tax revenues, raising the question of whether they are cost-effective. For example, according to the Legislative Analyst's Office, California's

R&D tax credit cost $545 million in foregone tax revenues in 2001-2002. Net Operating Loss Carry Forward provisions cost $450 million.[216]

Proponents of such incentives argue that they eventually pay off, both in terms of encouraging beneficial research and innovation, and ultimately in terms of economic growth and new sources of tax revenue. Do the tax incentives in fact have such results? This turns out to be a difficult question to answer. As the California Budget Project recently noted, tax incentives are not formally reviewed as part of the budget process and there is little if any data on their impact.[217] Only the R&D credit has received close analysis, and the results have been inconclusive.

In 1999, the California Council on Science and Technology commissioned a study on the effectiveness of California's R&D tax credit in spurring additional private-sector R&D investment. The authors concluded that a lack of data makes it difficult to answer the question, given the need to analyze the tax records and spending practices of individual firms.[218] The federal Office of Technology Assessment reviewed the federal R&D tax credit in 1995. It concluded that the tax credits probably did stimulate added R&D spending in direct proportion to the loss of tax revenue.[219]

According to a recent report by the California Budget Project, state and local taxes represent a small share of the total cost of doing business – typically less than three percent. At the same time, tax cuts can lead to reductions in spending on public services such as education and infrastructure, reductions that could in their own way inhibit the economic growth that the tax incentives are meant to spur.[220]

The Rationale for Government Subsidies and Public-Private Partnerships

State programs to promote a particular industry are sometimes subjected to a number of criticisms: that they involve the government in "picking winners" in the economy; that they foster a zero-sum competition among the states; and that they place an undue emphasis on industrial recruitment, or short-term job creation and retention.[221]

However, such efforts also often result in initiatives that have broad benefits. Public-private technology cooperation is backed by economists who believe that a free market will tend to under invest in research and development. The public-private partnership model is favored over simple subsidies so that the program will be more responsive to the realities of the marketplace and also to engage the private sector in funding and implementation.[222]

Government Regulation of the Bioscience Industries

We will briefly summarize here the main state and federal regulatory programs dealing with genetically modified organisms, pharmaceuticals produced through genetic engineering, and medical devices. For a fuller description of federal regulatory programs, see the Appendix.

FEDERAL REGULATION OF THE BIOSCIENCE INDUSTRIES

Food Safety

The mere fact that a plant or animal is genetically altered is not necessarily enough to trigger FDA regulation and a federal pre-market safety review. The FDA only regulates the product if it believes that the resulting food product differs significantly from conventional foods.[223]

However, the transgenic product could require a safety review if the added DNA causes the food product to differ in a way that could affect its safety or nutritional properties.

The FDA recommends that the developers of biotechnology crops consult with FDA and provide data about their product before commercialization to assure that the product in fact does not need to be regulated.[224]

If FDA decides that the food should be regulated, the manufacturer must provide convincing evidence of safety, such as additional studies of the effects on animals or humans. If the additive is approved, the FDA issues regulations governing its use and any labeling requirements. Federal officials will monitor the public's consumption of the additive, investigate complaints by consumers and physicians, and monitor new research on its effects.[225]

Food Labeling

There is no requirement for foods currently on the U.S. market to carry a label indicating whether they are genetically modified. The FDA could require labeling if genes were introduced from foods that are commonly allergenic (for example, a product using a gene from a peanut plant). In addition, FDA would require labeling of a genetically modified food product that it had determined would have significantly altered nutritional content.[226]

Safety and Effectiveness of Drugs and Biologics

Products made through genetic engineering are subject to the same type of scrutiny as conventionally-produced products. The Food and Cosmetic Act of 1938 and amendments require drug manufacturers to demonstrate both the safety and efficacy of new drugs, and required that drugs be produced according to specified manufacturing practice guidelines.[227]

After discovery of the potential medicine, the company conducts pre-clinical testing in animals and the laboratory. This is followed by a clinical trial process for FDA approval. Clinical trials are performed by the manufacturer, often in conjunction with universities or research institutions.

Clinical trials occur in three phases, culminating in randomized, double-blind studies. The trials are intended to assess toxicity, preferred dosage and delivery mode, risks of adverse reactions, and effectiveness.[228]

Review of Medical Devices

The FDA's medical device review process divides products into three classes, which are regulated with increasing degrees of strictness. Class I consists of products with minimal potential for harm to the user and simple in design (such as elastic bandages, enema kits, pipeting and diluting systems). Class II are moderate risk devices, such as powered wheelchairs and pregnancy test kits. Class III are devices that sustain or support life, are implanted, or pose potentially serious risks of illness or injury. These include pacemaker components and infant radiant warmers.[229]

Class II devices usually require a process known as Premarket Notification 510(k), and Class III devices require a process known as Premarket Approval. Premarket Notification 510(k) means that the device cannot be marketed until the applicant successfully demonstrates to the FDA that the product is substantially equivalent to one already in commercial distribution in the U.S. Premarket Approval is more involved and includes the submission of clinical trial data by the applicant.[230]

Device manufacturers comply with regulations intended to assure uniformity and reliability of every aspect of their design and production process. The FDA may also require manufacturers to track devices after they are sold. Manufacturers must develop procedures to identify and evaluate adverse events related to their devices, and to report these events to FDA. The FDA has the authority to recall products it believes to be harmful or suspend their sale.

Environmental Regulation of Transgenic Plants

The use of genetically modified plants is currently regulated by the U.S. Department of Agriculture (USDA), within the Agricultural Plant Health Inspection Service (APHIS).*

The review process focuses on whether the engineered plant could introduce a new, injurious plant pest or pathogen that could harm agriculture or agriculturally beneficial organisms.[231] The review is also governed by the National Environmental Policy Act (NEPA), which requires a broad assessment and public disclosure of the environmental impacts of federal agency actions and approvals.[232]

* The White House is currently proposing that APHIS be transferred from USDA to the new Department of Homeland Security. However, USDA intends to reorganize so that the APHIS biotechnology review function will remain at USDA in a new office called the office of Biotechnology Regulatory Services.

Based on experience over the years with issuing permits for various plants, APHIS has developed a list of low-risk plants and modifications that may be exempted from the permit requirement.[233] In such cases, a lengthy review of research data is not necessary.[234]

If a fuller review is required, the plant must undergo greenhouse and lab testing, after which the developer of a biotech crop applies to APHIS for a permit to cultivate it in contained field plots under conditions approved by APHIS.[235] Factors considered include the likelihood that the plant could outcross with a wild relative and transfer the new trait.[236]

Once sufficient data have been collected, the developers can petition APHIS for a determination that the plant should no longer be regulated as a plant pest.

EPA and Plant Pesticides

One of the most widely used forms of genetic modification has been plants that are resistant to pests or pathogens. Often these plants are genetically altered to produce their own versions of the natural pesticides normally produced by other kinds of organisms. The presence of a pesticide triggers regulatory oversight by the U.S. EPA.[237]

Pesticides must be registered with EPA, after the maker demonstrates that they do not have "unreasonable harmful effects" on humans and the environment. The maker must submit data that includes detailed information on the toxicology of the pesticide and how it is expected to behave in the environment.[238] EPA also sets maximum permissible food residue levels.

Field testing a transgenic pesticidal plant on more than 10 acres generally requires an experimental use permit. Tests are subject to monitoring and additional conditions intended to minimize the possibility that the plants could unintentionally enter the food or feed supply or persist in the environment.[239]

One commonly voiced concern about pest-protected crops is that they could rapidly cause harmful pests to become resistant to pesticides via natural selection (analogously to how over-use of antibiotics can create strains of resistant diseases). Accordingly, approvals for commercial use of such crops often include a resistance management program prescribing planting practices intended to reduce this danger.

EPA Regulation of Non-Pesticidal Microorganisms

Microorganisms containing genetic material from dissimilar source organisms are subject to review by the U.S. EPA before any environmental releases.[240]

EPA has adopted a two-level review system that provides stricter review for organisms deemed to pose higher risks. All "intergeneric" microorganisms, and microorganisms

derived from pathogenic sources, are subject to full review, while organisms that pose lower risks may receive an abbreviated review.

The full review process requires a risk assessment in which EPA will require information from the manufacturer on the source organisms, how they were manipulated, and their new traits. The risk assessment also generally requires data about the potential for human exposure, the environmental fate of released organisms, and human health and environmental effects. The applicant may need to provide information on the intended use of the organism, as well as proposed containment, mitigation and monitoring measures. EPA instructs manufacturers to assume that the microorganisms present a risk and to provide data demonstrating their safety.[241]

At the end of the review process, EPA may determine the risks are reasonable, unreasonable, or that there is insufficient information to evaluate the risk. The agency may require measures to reduce the risks to an acceptable level, prohibit the manufacture or use of the organism, or withhold approval pending the availability of better data.[242]

Laboratory Safety

Biotechnologists are expected to follow federal guidelines for safe laboratory practice when conducting research with microorganisms and DNA. Early fears that DNA research could accidentally unleash new human pathogens led to the formation of the Recombinant DNA Advisory Committee (RAC) of the National Institutes of Health in 1974. Although technically only guidelines, NIH's safety standards became a requirement for federally funded research. Private researchers almost uniformly followed suit, in part because adherence to NIH standards is widely presumed to provide protection against negligence liability.[243]

Criticisms of the Federal Regulatory Regimes

There are a number of criticisms that have been leveled at the federal regulatory processes from a variety of perspectives.

Regulatory Compliance Costs

The FDA has long been criticized for a lengthy, expensive review process that many companies complain inhibits innovation. The FDA Modernization Act (FDAMA) of 1997 required the FDA toagree to implement programs that would accelerate the drug development process. According to the Biotechnology Industry Organization (BIO), the reforms have been helpful but progress has stalled due to insufficient funding. Says BIO, "Potential investors need to know that products from biotechnology companies will get a timely and high quality review from the agency. Without this assurance investors would be reluctant to invest and thus research and development could be hampered."[244]

Agricultural biotechnology interests have also criticized the regulatory process for transgenic crops and foods. They have argued that there is a lack of coordination between the various federal agencies, regulatory inconsistency, regulatory scrutiny that is

out of proportion to risks, and excessive costs to comply with testing and paperwork requirements. They note that paperwork and testing required by USDA for transgenic organisms is 10-20 times more expensive than analogous requirements for virtually identical organisms modified with conventional techniques.[245]

Ensuring Food Health and Safety

As already noted, there has been considerable controversy about the safety of genetically modified food.

Even some scientists who believe current transgenic foods are safe have questioned whether the federal regulatory system can adequately assess the potential risks in the future, given the number, variety, and complexity of genetic modifications that could eventually be introduced to the marketplace.[246] For example, a recent report sponsored by the nonpartisan Pew Initiative on Food and Biotechnology concluded that federal research programs were spread too thinly and too poorly coordinated to produce timely allergenic risk assessments for the diverse biotechnology foods now under development.[247]

Furthermore, there is little if any long-term research or monitoring to determine the health effects of these products once they are in the food supply.[248] The system has also been criticized for lacking clear rules to guide the industry as it develops new products, and for lacking sufficient provisions for public input.[249]

An international panel of scientific bodies coordinated by the National Academy of Sciences recommended that regulatory agencies in every country establish systems to identify and monitor the long-term health impacts of genetically modified foods, and to share information with the goal of developing standardized methods of risk assessment.[250]

The biotechnology industry would likely oppose stricter requirements for testing genetically modified foods, as it already criticizes the regulatory programs for imposing substantial compliance costs.

The Food Labeling Debate

There has been considerable controversy over whether the government should require genetically modified foods to be labeled as such. Advocates of labeling say it would allow consumers to choose whether they wish to avoid the risks of consuming GM foods. However, supporters of GM food argue that such labels would wrongly imply that genetic modification was dangerous. They say mandatory labeling would hurt sales, impose needless costs and unnecessarily alarm the public. If there are consumers who are worried about GM food, they should (according to this viewpoint) be willing to pay a premium for special products that have been labeled as GM-free (in a fashion similar to the current marketing of products labeled organic).

The Bush administration has stated that it does not support mandatory labeling of genetically modified foods, saying it would needlessly frighten consumers and wrongly imply that such foods are unsafe.[251]

Due to the widespread concerns in export markets about genetically modified food, USDA is considering, with industry support, a voluntary system whereby crops could be certified as being GMO-free. The certification would be based on information provided by companies about how they keep their products separate from gene-altered crops throughout the food production chain.[252]

In Oregon, a ballot initiative requiring mandatory labeling of transgenic crops and food will be placed before the voters in November.[253] Activists behind the campaign say a similar effort would likely follow in California should the Oregon measure be successful.[254]

Protecting the Environment

The controversy over whether Monarch butterflies are harmed by Bt corn provides a telling illustration of the gulf between supporters and opponents of GMOs. Supporters of biotechnology pointed to this episode as a vindication – the purported threat from the Bt pesticide turned out to be far less severe than initially feared. On the other hand, critics of GMOs pointed out that at least one variety of Bt corn did pose a risk, and that the federal regulatory process had completely overlooked the issue in its original approval of the corn.[255]

A panel of the National Academy of Sciences recently reviewed the federal regulatory process for genetically modified plants. While the panel noted that serious environmental problems had not yet occurred, it was possible for transgenic plants to have unanticipated ecological consequences. The panel recommended that the regulatory review process be improved by the addition of more independent scientific input and a strengthening of the ecological expertise within the USDA's staff. The panel recommended more long-term monitoring to detect adverse effects and refine the review process.[256]

A Regulatory Gap: Genetically Modified Animals

There appears to be a gap in federal regulations when it comes to transgenic animals such as insects and fish. The most serious risk would probably be from animals that were difficult to contain and could escape and spread if released into the environment, such as fish or insects.[257] For example, transgenic fish are thought by some scientists to pose risks of interbreeding with wild fish, with some hypotheses suggesting the wild relatives could be driven to extinction.

Many commercial uses of transgenic animals are under development. For example, a genetically altered Atlantic salmon that will grow faster and consume less food than its wild relatives has been developed by a Massachusetts company called Aqua Bounty. Researchers have patented transgenic catfish and carp that contain a silk moth gene that produces a natural compound that kills fungi and bacteria.[258]

The FDA is apparently asserting regulatory authority over a wide variety of transgenic animals under the theory that genetic modification is a "new animal drug" governed by the animal drug provisions of the Federal Food, Drug, and Cosmetic Act (FDCA). The FDA asserts that its mandate includes environmental impacts to the extent that they adversely affect the health of humans or animals.[259]

The FDA's assertion of authority seems questionable. Neither the governing statute nor the agency were designed to address wildlife and ecological management. Similar questions could perhaps also be raised about whether the U.S. Department of Agriculture, operating under a law intended to address agricultural pest control, should have primary authority for evaluating the potential ecological effects of all transgenic plants.

The National Environmental Policy Act (NEPA) provides some additional environmental review requirements. However, as a National Academy of Sciences report recently noted, there seems to be a potential conflict between NEPA, which is intended to provide full public disclosure and input, and FDCA, which keeps the "animal drug" licensing process confidential until the product is approved.[260]

STATE GOVERNMENT'S ROLE IN REGULATION

The regulation of health, safety and environmental issues relating to biotechnology occurs mainly at the federal level. No state agency is explicitly responsible for evaluating or tracking the effects on human health or the environment associated with transgenic organisms.[261]

Drugs and Medical Devices

The California Department of Health Services (DHS) shares responsibility with the U.S. FDA for regulating the manufacture of drugs and medical devices, inspecting and licensing all such facilities in the state. DHS ensures that the facilities conform to the extensive federal regulations for good manufacturing practice and quality control.[262] DHS has the power to block the sale of products that are impure, mislabeled, adulterated, or unsafe. It coordinates closely with U.S. FDA in this area, but takes a leading role because it has stronger and faster enforcement mechanisms, including the ability to pursue criminal investigations.[263]

In theory, it is possible for companies seeking approval of a drug or medical device to apply to the California Department of Health Services for approval under California's Sherman Food, Drug and Cosmetic Law rather than to the Federal FDA.[264] However, such applications are rare, as FDA approval allows the product to be sold throughout the entire United States, not just California.

Genetically Modified Food and Crops

In general, the state defers to the federal government when it comes to assessing environmental or human health issues associated with genetically modified crops and food.

In 2000, the Legislature asked the Office of Environmental Health Hazard Assessment to report on its efforts in evaluating potential health and environmental hazards from genetically modified organisms. OEHHA replied that it had no oversight authority over safety of genetically modified foods.[265] The Legislative Analyst's Office (LAO) noted that OEHHA "lacks both the resources and the direction to track, evaluate and assess the potential human health effects of GMOs."[266] LAO recommended that funding be provided for these purposes.

The California Department of Food and Agriculture for the most part defers to the federal government in evaluating the environmental aspects of field tests or commercialization of genetically modified crops. Under federal regulations, the Department is notified of proposed field tests of transgenic crops. CDFA can review and provide input on the permits. It has authority to inspect facilities, field test sites, and records.[267] However, the Department restricts its role to issues relating to the introduction of agricultural pests. For example, if a transgenic crop were to be tested using an imported agricultural pest, CDFA might place restrictions on the use of the pest organism to prevent its spread.[268]

Because some genetically modified crops are engineered to produce their own pesticides, the California Department of Pest Regulation could conceivably become involved. In 2000 the Legislative Analyst's Office recommended funding CDPR to have a staff toxicologist position to review and evaluate submissions for registering pesticides based on biotechnology such as Bt crops.[269]

DPR has not, so far, required registration of plant pesticides in California. The Department does not view Bt toxins as having hazardous impacts, and notes that such products are not yet widely used in California. In addition, the Department seeks to coordinate with federal regulatory programs, and is taking a wait-and-see approach to what it considers an unsettled and controversial area of federal regulation.[270]

Transgenic Animals

The state's Fish and Game Code and regulations prohibit possession of animals listed as "restricted" nuisance or exotic species without a permit from the California Department of Fish and Game. Transgenic plants and animals could conceivably be added to these lists.

The California Department of Fish and Game also has statutory authority to inspect and register aquaculture facilities and to regulate the importation of aquatic plants and animals for aquaculture. The Department may prohibit any aquaculture operation it determines would be detrimental to wildlife. This would seem to give the Department some authority to regulate transgenic animals imported for aquaculture.[271]

Segregation of GM and Non-GM Rice

The California Rice Certification Act of 2000 (AB 2622, Dickerson) established a special committee to develop rules that would allow the certification of rice as being free of "characteristics that may adversely affect the marketability of rice in the event of commingling with other rice." This certification could be used to reassure buyers that rice is not tainted by plant diseases or pests. But it would also likely be used to certify some rice as being 'GMO-free.'[272]

Vandalism of Genetically Modified Crops

A bill passed in 2000, AB 2510 (Thomson) attempts to deter anti-biotechnology activists from vandalizing genetically modified crops. Protesters have destroyed a number of experimental crops at UC Davis and elsewhere. The new law imposes fines of twice the value of the crop damaged or destroyed.

Genetic Privacy

California law requires written consent before information from a genetic test can be disclosed.[273] Federal law prohibits health insurance discrimination based on any "health status-related factor," including genetic information, for group health plans. California law additionally prohibits health insurers from establishing rules for eligibility based on genetic testing, and forbids the requirement of genetic testing as a condition of coverage or for risk classification purposes.[274] California law prohibits employment discrimination based on genetic test results or information about genetic testing. Employers are also prohibited from performing genetic tests on employees.[275]

THE DEBATE OVER CLONING AND STEM CELLS

In 1997, after the cloning in Great Britain of a sheep named Dolly was hailed as a breakthrough, President Clinton asked the National Bioethics Advisory Board (NBAC) to study the cloning issue. NBAC concluded that adult-cell cloning techniques were too risky for use on humans, and recommended a five-year moratorium.[276] This year, President Bush's Council on Bioethics issued a divided report, with a majority favoring a moratorium on research using cloned embryos, and a minority saying such research should be allowed with proper oversight.[277]

To date, no federal moratorium has been enacted. However, the scientific community has adopted a voluntary moratorium on reproductive cloning in the United States.[278]

In August 2001, President Bush issued an order that federal funding for research using embryonic stem cells be limited to existing stem cell lines. The decision has been controversial, with experts disagreeing over whether the number of qualified cell lines is adequate for researchers' needs.[279]

In Congress, a bill known as the Brownback-Landrieu Human Cloning Prohibition Act (S. 1899), supported by President Bush, would ban all forms of human cloning and has passed the House of Representatives. If the bill passed, federally funded stem cell research on existing cell lines could continue under President Bush's August 2001 policy, but the creation of new stem cell lines through cloning would be banned altogether. A rival bill backed by the bioscience industry, the Specter-Feinstein Human Cloning Prohibition Act of 2002 (S 2439), would prohibit reproductive cloning but allow embryonic stem cell research to continue.[280]

Dolly, the first cloned sheep, and progeny Bonnie. (Roslin Institute, Edinburgh).

In 1997, California's legislature passed a temporary ban on human reproductive cloning through 2003. At the same time, the state established an advisory commission on human cloning to monitor this law, hold hearings, and report back to the legislature. In December 2001, the commission recommended that California maintain its ban on human reproductive cloning while continuing to permit the cloning of human embryos for therapeutic research.[281]

These recommendations have recently been put into effect by the Legislature. One bill passed during the past session, SB 1230 (Alpert), extends the ban on human reproductive cloning indefinitely. It also requires the state Department of Health Services to establish a committee including bioethicists to advise the Legislature and the Governor on human cloning and other issues relating to human biotechnology. Another measure, SB 253 (Ortiz), declares it to be the policy of the state to allow human embryonic stem cell research. In addition, SCR 55 (Ortiz) creates a panel to advise the Legislature on stem cell research, co-chaired by the chairs of the Senate Committee on Health and the Human Services and the Assembly Committee on Health.

Religious and anti-abortion groups have supported a ban on both reproductive and therapeutic cloning (cloning embryonic stem cells for research). Representatives of the bioscience industry, as well as some women's and health care organizations, have supported bills allowing continuing therapeutic cloning and stem cell research.

A Menu of Policy Alternatives

In this section, we will review a wide variety of policy proposals put forward by the interest groups, economic development specialists and government agencies interested in the bioscience industries in California. My purpose is not to endorse any of these proposals, but rather to provide an overview of the proposals that would likely arise if the state were to begin a serious discussion of a bioscience strategy. These proposals provide a sort of preview of what the menu of possible initiatives might well look like once such planning got underway.

OVERVIEW OF ECONOMIC DEVELOPMENT POLICIES

Most of the policies pursued by state and local governments with respect to the biosciences are intended in one way or another to promote the growth of these industries. Before looking at the specific proposals made in California, we will review the general types of bioscience development initiatives most commonly pursued by states throughout the country, including California. The Biotechnology Industry Organization published a survey of state initiatives in the biosciences in 2001.[282] These were the common themes that emerged from many states.

Bioscience research facilities. California and several other states are using state funding for bioscience-related research centers, including the construction of facilities and labs and the purchase of equipment, with the hope of attracting both research talent and federal funding. The state-funded facilities often involve partnerships between industry, universities, and state government.[283] California is pursuing such an approach with its new Institutes for Science and Innovation focused on biosciences and nanotechnology. Several states have used tobacco settlement dollars to increase funding of biomedical research.[284]

Research parks and incubators. Nine states reported research parks focused exclusively on bioscience companies, with a number of others in planning stages. Fifteen states reported bioscience incubators, and 19 reported technology incubators that include wet lab space.[285] As already noted, several such initiatives are underway in California. The impetus for these has tended to come from the regional level rather than the state government so far.

Commercialization and business development support. Most states have centers intended to provide technical support, information, and networking for companies needing assistance with commercialization and business development. In California, the Regional Technology Alliances provide such services. A few states, such as Maryland, have centers specifically targeting biotechnology.[286]

Publicly funded seed and venture capital investment. Twenty-eight states reported having publicly supported seed or venture funds that can invest in bioscience companies, and five have funds investing exclusively in such companies.[287] The biotechnology investment fund of California's Public Employees' Retirement System (CalPERS) is an

example. However, CalPERS may not be as able to make risky investments as some of the venture funds in other states, since, as a retirement fund, CalPERS has a fiduciary responsibility to state employees.

Tax incentives. The majority of states have R&D tax credits, and many states offer sales and use tax exemptions and investment tax credits.

Workforce development. Initiatives include establishing new two-year associate degree programs, and collecting input from companies on training and educational needs.[288]

State Biotechnology Industry Specialists. Several states have hired dedicated professional staff to assist the bioscience industries with financial, regulatory, and other programs.[289]

CURRENT PROPOSALS TO ASSIST THE BIOSCIENCE INDUSTRIES IN CALIFORNIA

Bioscience advocates, economic development experts and government agencies have proposed many ideas for assisting California's bioscience industries. Many of them are variations on the themes summarized above.

Tailoring Tax Incentives to Help the Bioscience Industries to Grow

For many bioscience companies, existing tax incentives may not be useful because they are based on credits or deductions applied to income. With their lengthy, costly product development cycles, many younger bioscience companies lack revenues and are unable to exploit these incentives. Accordingly, bioscience advocates often recommend that tax incentives should be restructured.

Among the proposals that have been put forward:[290]

Increasing the Net Operating Loss (NOL) carry forward period. A longer carry forward period increases the chance that a company will begin earning revenues before it loses its opportunity to use its net operating loss deduction. Some states have longer carry-forward periods than California's 10-year period. For example, New Jersey has an NOL carry-forward of 15 years, and Connecticut and Texas allow carry-forwards of 20 years. Due to California's revenue shortfalls, the recently enacted state budget suspends NOL carry-forward for two years, although companies will be compensated with a two-year extension of the maximum NOL carry-forward period.

Tradable or Refundable Tax Credits. Biotech companies would be allowed to cash in on tax incentives by allowing them to be sold to other companies or to make them into refundable credits. Three states, Connecticut, Hawaii, and New Jersey, allow firms to transfer or sell unused R&D tax credits or net operating loss (NOL) carry-forwards.[291] There have also been proposals to legislate this at the federal level.[292]

Capital Gains Tax. The Biotechnology Industry Organization has urged cuts in capital gains taxes as a way to encourage investment in biotechnology.

Business Income Tax Apportionment Formula. Industry advocates are calling for changes to California's apportionment formula used to calculate business income taxes. The current formula takes into account property, payroll and sales in the state. The proposal would change this to a single-factor formula based exclusively on sales (which would reduce taxes for corporations with significant property and payroll in California.) Proponents argue that the existing formula creates a disincentive for companies to expand in California.

High Technology Capital Gains Exclusion. A bill introduced in the last legislative session, AB 2358 (Bates 2002), would have provided a gross income exclusion for any gain from the acquisition, sale, or exchange of a stock option in a qualified high technology business located in this state. The bill died in committee.

Infrastructure Improvement

Bioscience industry supporters often point out that California's infrastructure problems make it more difficult and costly to do business, and can deter venture capital from flowing into the state.[293*] The California Economic Strategy Panel reached similar conclusions.[294]

The following are the major infrastructure issues that have been highlighted by bioscience advocates and company executives:

Electricity. Bioscience companies often use a great deal of electricity, and reliability of the supply may also be important for sensitive laboratory or manufacturing processes. Supporters of the industry advocate taking action to reduce electricity costs and expedite the development of new capacity.[295]

Water. As with electricity, the cost and reliability of the water supply is a concern to firms that rely on water in their laboratory processes or manufacturing. This issue is particularly of concern in southern California.[296]

Transportation and Traffic. Leaders of both the San Diego and Bay Area bioscience industries are concerned about the state's traffic and transportation problems. Industry organizations and leaders in both regions have called for improvements in freeway traffic flow, more mass transit, and development of regional air transportation plans.[297]

Some ongoing efforts to address these concerns at the state level deserve mention. The Governor's Five Year Infrastructure Plan, mandated by state law,[†] is a comprehensive plan for state investment in infrastructure that must be submitted annually with the state

[*] The gap between the state's population growth rate and the growth in capitol outlays has been growing since the 1950s. Recent estimates of the gap between infrastructure funding and needs have ranged from $82-90 billion over the next 20 years. See California Commission on Building for the 21st Century, *Invest for California: Strategic Planning for California's Future Prosperity and Quality of Life*, February 27, 2002.

[†] Chapter 606, Statutes of 1999.

budget. The 2002 plan proposes spending $56 billion over the next five years on infrastructure, including transportation, education, water supply, the environment, and public safety.[298]

Easing Land and Housing Shortages

Although the cost of housing is a major concern for bioscience companies in the Bay Area and San Diego, leading to industry calls for state and local government to make this a higher priority.

With regard to shortages of industrial land and space for facilities, the Los Angeles Regional Technology Alliance has called for civic leaders to reduce the legal and administrative hurdles for developing land to establish biotech corridors or campus-style bioscience parks.[299] In San Diego, the county's new biotechnology action plan calls for the county to address the lack of suitably zoned, developable industrial land through the General Plan update process.[300]

Grants and Financial Assistance to Companies

There are relatively few sources of financial assistance for companies to advance from research that demonstrates a product's potential to commercialization and marketing of a product. For instance, young bioscience companies may be unable to afford the manufacturing facilities necessary to make prototypes or test runs of products for clinical trials. The Biotechnology Industry Organization says that states should help make shared manufacturing facilities available to such early-stage companies.[301] The costs to build a biotechnology manufacturing facility can be prohibitively high, but such a facility could be used by a number of companies making more than one product.

While California is among the states offering tax credits for such purposes, some states also offer loans or other financing mechanisms. For instance, Connecticut's Biotechnology Facilities Fund is a $60 million fund dedicated to helping biotechnology companies with the construction of wet laboratory space and related facilities.[302]

Some in the industry have called for California to provide research and development grants analogous to the federal Small Business Innovation Research (SBIR) program. The state could either offer its own grants or provide matching funds for federal SBIR grants.[303]

Support for Clinical Trials

Some in the industry say that it can be hard to find facilities and support for testing new technologies. They have recommended state funding of public health and other labs to participate in these kinds of trials.[304] The Biotechnology Industry Organization and biotech executives surveyed by the Bay Area Bioscience Center have recommended that states assist mid-stage companies with low-interest loans to help them finance clinical trials.[305] It should be noted that such loans could be fairly risky for the lender, since only one in five drugs entering clinical trials is ultimately approved.[306]

University Research and Technology Transfer

As noted earlier, the University of California system has been criticized for procedures and rules that can make it difficult to commercialize promising inventions and discoveries created by UC faculty. The UC system has taken some major steps to make its technology transfer programs more effective. A UC task force that examined the issue in 2000 identified a number of continuing high priorities. These included training and recruiting technology transfer staff; developing new web and database tools to help companies and faculty to interact; more analysis of the economic impact of UC-industry interactions; and further review of University policies governing research relationships with the private sector.[307]

Science Education and Workforce Training

As noted earlier, many in the industry and the economic development community are concerned about the capability of California's educational system to produce enough skilled science and technology workers and researchers.

Recommendations to improve California's bioscience workforce fall into three categories: basic science education, vocational training for non-research professionals, and the training of scientists.

The bioscience industry would probably be willing to lend assistance in developing and implementing such programs. For example, in San Diego, bioscience companies have offered internship opportunities, scholarships, donated equipment, and advice to schools.[308] Several community college programs have benefited from donated equipment and from industry input about the industry's training and workforce needs.

Basic Science Education

Economic development experts and bioscience advocates have called for greater emphasis on the biosciences at the K-12 level to prepare and motivate students for bioscience careers.[309] They have also called for support of science-oriented charter and magnet schools[310] and the creation of more internship opportunities.[311]

According to the California Council on Science and Technology, there is a need for more female and minority role models to help remedy gender and ethnic enrollment gaps in college science and technology programs.[312]

Vocational Training

Many bioscience advocates have called for a greater emphasis on training the non-research bioscience workforce – skilled technicians, regulatory specialists, and others who can help maturing companies to manufacture and market their products. Accordingly, they call for expansion of community college programs that provide math and science education. Students could be prepared to enter the field through specialized

professional degrees or certificates geared to the specific workforce needs of the bioscience industries.[313]

According to EdNET, the community colleges' economic development program, there are a number of challenges faced by the community colleges in their efforts to train the biotechnology workforce: 1) access to sufficient state-of-the-art equipment, which is "startlingly expensive;" 2) lack of knowledge in the community (high schools, industry, the local workforce) that the training is available; and 3) insufficient numbers of faculty members.[314] The California Council on Science and Technology (CCST) recently also noted that limited laboratory and facility resources, science teachers, and counseling services hamper science education in the community colleges.[315]

Furthermore, CCST has recommended greater collaboration between community colleges and four-year colleges in order to assure that community college students have access to necessary science and engineering courses. CCST has also suggested that it might be necessary to pay community college science and engineering faculty higher salaries than other disciplines, since they can command higher salaries in the private sector.[316]

An area that has yet to attract much attention is the continuing education of professionals after they join the workforce. Such programs are offered by the University of California, community colleges, the California State Universities, and private institutions. The California Council on Science and Technology has noted that these programs enjoy very high enrollments and are likely important to maintaining a high-quality technology workforce. CCST recommends assigning a state entity to comprehensively analyze the state's continuing education system.[317]

Training Scientists

The large number of H-1B visa holders suggests that California should emphasize training its own scientists so as to reduce the need to import talent from out of state or abroad. According to BIOCOM/San Diego, the public universities will need increased funding to train the necessary numbers of students and to deal with deferred maintenance and upgrading of aging equipment and facilities.[318]

State-Level Dedicated Staff to Assist Bioscience Companies

During Assembly hearings on biotechnology last year, some executives suggested the state assign designated personnel to help companies deal with regulatory and other government programs affecting the industry.[319]

In the Biotechnology Industry Organization's 2001 report on state bioscience initiatives, 12 states reported having staff dedicated to working with biotechnology industries, with duties such as coordinating biotechnology initiatives, assisting companies with regulatory issues, and encouraging companies to locate in the state.[*320] California's Technology,

[*] These states were Delaware, Georgia, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Mexico, Ohio, Utah, and Virginia.

Trade and Commerce has staff who perform a similar role, although they are not exclusively dedicated to working on bioscience issues.

PROPOSALS REGARDING THE REGULATION OF THE BIOSCIENCES

Regulation is an important factor in the biosciences world, and there is a lively debate between those who want more regulation and those who think current regulations are strong enough.

Regulation of the Release of Transgenic Organisms

The release of transgenic organisms into the environment is presently regulated at the federal level. Many critics believe that the federal regulatory system is not adequate. The range of proposals put forward includes:

- Stronger requirements for testing and risk assessment before releasing transgenic plants and animals.
- More monitoring of the environmental impacts of transgenic organisms already released.
- A moratorium or ban on releasing transgenic organisms.

For example, a recent bill that was passed by the California State Senate during the last session (SB 1525, Sher) would have prohibited the importation or possession of transgenic fish in the state without a permit. The bill died in the Assembly.

Regulation of Genetically Modified Food

As with the environmental impacts of biotechnology, the voices for change include activists calling for a total ban, as well as calls for more modest, incremental refinements of the federal regulatory system. Many critics also call for the government to require that foods containing genetically modified ingredients bear special labels. For the most part this debate has so far focused on federal policy rather than proposals for new state-level regulation. As noted earlier, the Legislative Analyst has called for the state to fund studies of the human health effects of GMOs.

Restrictions on Cloning and Stem Cell Research

Human reproductive cloning has been banned in California and is likely to be banned federally as well. However, as noted earlier, there are some who harbor deep misgivings about embryonic stem cell research and would like to see further restrictions or a ban. As noted earlier, California's governor recently signed legislation permitting stem cell research.

Regulatory Relief

There are a number of areas where the bioscience industries are lobbying government to either ease regulation or else reject proposed regulation. These include:

- *Cloning and stem cells*. Bioscience advocates tend to oppose laws that would prohibit therapeutic cloning and stem cell research.
- *Water pollution control*. In San Diego, the county is interested in finding ways to offer the biosciences and other industries flexibility in meeting stormwater pollution control requirements.[321]
- *Price controls*. Bioscience advocates tend to oppose proposals that would limit the prices of pharmaceuticals.[322*]

Low-Level Radioactive Waste Disposal

Some medical bioscience companies use radioactive materials in their research, and are worried about the costs of disposing of radioactive wastes. Backers of the industry support opening the controversial and long-delayed Ward Valley low-level radiation storage facility, or finding an alternative in-state facility. A bill passed this year, AB 2214 (Keeley), effectively rules out Ward Valley as the site for the state's radioactive waste repository.

Some in the biotechnology industry were worried about legislation that tightened the rules on disposal of low-level radioactive waste (SB 1970, Romero 2002). Opponents claimed the measure would create unreasonable obstacles for companies using radioactive materials in biomedical research to lease or de-commission their facilities. The bill was vetoed by the governor. Another bill that encountered bioscience industry opposition (SB 1444, Kuehl 2002) proposed new requirements for cleanup prior to the sale or lease of a site where radioactive materials had been used. It stalled in the Assembly.

[*] For example, industry advocates have come out against AB 1853 (Koretz), which would impose price controls state purchases of pharmaceuticals based on how much drug companies expend in marketing them.

Toward A Bioscience Strategy for California

What should be California's approach to the bioscience industries? Should the state be more active in promoting the bioscience industries, or do so differently? The state has three basic options. It can maintain the status quo. It could make incremental modifications, perhaps picking and choosing from the proposals described in the preceding "menu" of policy options. Or, it could engage in a strategic planning effort to assess where the state stands and what it should do.

In this section we will talk about the third option – what would be involved in developing a bioscience strategy.

WHAT IS A BIOSCIENCE STRATEGY?

According to a survey by the Biotechnology Industry Organization, as of 2001 ten states had developed or begun developing "a biotechnology or life sciences strategic plan" during the last four years. Several other states have technology strategic plans that include a bioscience focus.[323]

What is Strategic Planning?

What distinguishes a "strategy" from ordinary policy initiatives? In contrast to incremental policy making, developing a strategy generally implies a systematic assessment of current assets and needs, the setting of goals, and adoption of a long-range plan.

A strategy might require a major new commitment of resources from a state that already has many competing priorities. And, it could result in a reorganization or redirection of many existing programs and resources. As a result, a strategic plan will need to motivate and coordinate a variety of actors and agencies in a common pursuit. This in turn may necessitate considerable consensus-building during the planning process. Developing the plan might involve participation by not only the executive and legislative branches but also academia, industry, and other interest groups representing consumers, environmentalists, labor, and so forth.

The input and cooperation of the industry would help ensure the plan is responsive to business realities, and it may also be vital to leverage public dollars with private resources. When enlisting industry, planners must be mindful that the bioscience industries are not monolithic. For example, the interests of medical biotechnology companies are not always the same as those of medical device firms or agricultural biotechnology companies. The needs of small startup companies trying to survive until they have a marketable product are not the same as those of large, mature companies looking to expand.

Lessons From Other States

During the 1990s, the U.S. Economic Development Administration canvassed science and technology plans and planners in all 50 states, and derived a set of "best practices." The study concluded that strategic planning should do the following:[324]

- Enlist a "champion" with the ability to bring all of the relevant players to the table and promote the implementation of their recommendations.
- Obtain wide range of viewpoints.
- Take into account the needs of all the state's regions.
- Build on existing delivery systems.
- Include performance indicators related to outcomes (rather than inputs).
- Assign responsibilities and timelines in the implementation plan.
- Tie goals and objectives to the state budgeting process (for example, include provisions to require that new initiatives in a given department are consistent with the strategy).

A Few Examples of Bioscience Strategies in Other States

The governor of Texas recently announced formation of a Governor's Council on Science and Biotechnology Development. The Council will include academics, the business community, and government officials. The governor has asked the council to identify ways that institutions of higher learning can coordinate efforts to attract federal funds, develop a strategy to increase public and private R&D expenditures, and identify ways to commercialize intellectual property.[325]

In Virginia the governor has created a 30-member advisory commission that is supposed to spend five months examining the question of how to promote the state's biotechnology industry. The commission includes lawmakers, state and local economic development officials, and company executives, and was to begin meeting in July 2002.[326]

Michigan has established a process in which the governor and legislature set a broad policy agenda, and are leaving the implementation to academia and industry. The state has enacted legislation that calls for establishing a biotechnology industry cluster (the "Michigan Life Sciences Corridor.") The development of the Corridor is anticipated to be a 20-year, $1 billion project. Using tobacco settlement funding, the state will fund research projects at universities, public and private research institutions, and companies. Research proposals will be evaluated through a process modeled on the National Institutes of Health, with 100 scientists around the country taking part in reviewing proposals. A steering committee including Michigan university presidents and private industry executives will approve final funding decisions.[327]

CALIFORNIA PRECEDENTS FOR BIOSCIENCE PLANNING

Unlike some other states, California does not currently have any comprehensive statewide strategy for the bioscience industries. In this section we will review California

state government's past and present efforts to address the challenges and opportunities posed by the biosciences.

California Commission on Industrial Innovation

Created by legislation in 1982, the Commission was established under the direction of the Governor's Office to help develop policies to foster California's economy. Biotechnology was one of the industries targeted. The Commission included representatives of California government, academia, labor, and industry.

The Commission's focus on biotechnology was prescient but premature. A study sponsored by the Commission concluded that biotechnology was still in its infancy, "not really a full-fledged industry yet." In terms of public policy, the study concluded that "there seems to be no reason to attempt to encourage the industry by supplying incentives that it neither needs nor wants."[328]

Interagency Task Force on Biotechnology

In 1985, Governor Deukmejian signed an executive order creating an interagency task force on biotechnology. The task force was supposed to evaluate the effectiveness of the existing statutes and programs in tracking and regulating the growing biotechnology industry.[329] In 1986 the task force published a report describing California's regulations and permits relating to biotechnology.[330] The task force later issued a report on food labeling. It concluded there was no reason for special labeling of biotechnology foods, and recommended instead a program of consumer education.[331]

Governor Wilson's Council on Biotechnology

In 1993, Governor Wilson signed an executive order creating the Governor's Council on Biotechnology. Comprised of industry representatives, the council advised the Administration on issues of concern to the industry and ways to promote the biotechnology industry in California. It consisted of 16 members that were CEO's of California biotechnology companies and met quarterly.[332]

California Economic Strategy Panel

In 1993 Governor Wilson signed AB 761 (Vasconcellos), the California Economic Development Strategic Planning Act of 1993. The Act created the California Economic Strategy Panel, which is supposed to convene biennially to "develop an overall economic vision and strategy to guide long-term policy affecting our economy."[333] The panel, convened by the Secretary of Trade and Commerce, includes members appointed by the Governor and Legislature.

After carrying out research and sponsoring forums in several regions of the state, the Panel produced an economic strategy report in 1996. Healthcare technology was one of several key industries the strategic analysis focused on. It concluded that there were three main public policy areas that "profoundly affect the capacity and prospects of

California's businesses to prosper and economy to grow:" 1) workforce preparation, 2) education, and 3) taxation, regulation, infrastructure and quality of life.[334]

The Economic Strategy Panel became dormant after its initial work. It was recently revived in order to resume its legislatively mandated biennial cycle of reviewing the California economy and rendering policy recommendations, and the Trade, Technology and Commerce Agency is continuing to provide support although it has not received any funding in the current budget for that purpose.

Food Biotechnology Task Force

The Food Biotechnology Task Force was created by the Legislature in 2000 (SB 2065 Costa). The Task Force is co-chaired by the California Health and Welfare Agency, the California Technology, Trade and Commerce Agency, and the California Department of Food and Agriculture.

The Task Force is supposed to report to the Legislature by January 1, 2003 on the benefits and impacts of food biotechnology, as well as the existing federal and state evaluation and oversight procedures. An advisory committee advising the Task Force includes representatives from consumer groups, environmental organizations, farmers, ranchers, the biotechnology industry, researchers, organic farmers, food processors, retailers, and others. The California Council on Science and Technology is preparing a scientific literature review as well.

Conclusions

California's economic strength has long been dependent on its leadership in technological industries. California is the nation's leader in the bioscience industries, a set of industries that most observers agree are developing the power to reshape society and the economy in profound ways. These changes are occurring rapidly, and California should be ready to respond to and anticipate them.

Although many other states are aggressively promoting these industries, California can boast a wide diversity of programs and initiatives of its own. However, California does not have a comprehensive strategy for the bioscience industries. Given the growing importance of these industries, the diverse challenges they face, and the strong interest of many other states in competing for leadership in these fields, California should consider developing such a strategy.

Any ambitious new plan for changing the state's role would require broad-based support. To gain this would likely require a systematic effort to assess the state's needs and goals and weigh the views of a variety of stakeholders in and outside of government. Input and participation by a broad array of interests could help to navigate through potentially controversial issues. At the same time, the plan development process can be an opportunity to enlist the involvement and support of influential parties (business leaders, local government, state policy makers, and others).

A strategy for the bioscience industries must take into account the controversies and public concerns about the safety, environmental impact, and ethical implications of these technologies. There will continue to be calls to expand or constrain the state's regulatory role. Even those whose sole goal is the growth of the bioscience industries cannot ignore such issues. Regulations have a major influence on the bottom line of bioscience companies.

One of main questions a strategic planning process must address is whether California commits sufficient resources to providing incentives and economic development assistance to these industries. California's efforts are no doubt significant. But California is, willingly or not, involved in competition to provide incentives with many other states.

The question of whether California is doing enough is to a large degree a political question about how to allocate resources. A systematic, broad-based planning effort could help convince the public that the policies in a biosciences strategy represented part of a rational plan for the state's economy, rather than an exercise in favoritism or "picking winners."

At the same time, it should also be noted that many of the policies called for by the bioscience community would unquestionably have broad benefits for businesses and the public beyond the bounds of the bioscience industries. Many other industries and the general public suffer the effects of infrastructure deficits, traffic, under-funded schools,

and shortages of affordable housing. Improvements in science education have benefits that go beyond boosting the workforce for a particular industry. Although some of these issues are too large to be solved within the framework of a biosciences plan, such a plan could have the ancillary benefit of advancing the debate about the state's infrastructure needs and goals.

In support of a strategic planning effort, it would be useful to more fully document the benefits the bioscience industries are bringing to the state, in terms of jobs, tax revenues, and stimulation of other industries. At this point, reliable, objective statistics about the bioscience industries are difficult to obtain. In addition, more could be done to document how and to what extent California's existing programs and incentives actually help the bioscience industries. We should consider whether our efforts will create measurable outcomes we can use to assess and refine our strategy as the bioscience industries continue to evolve and grow.

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